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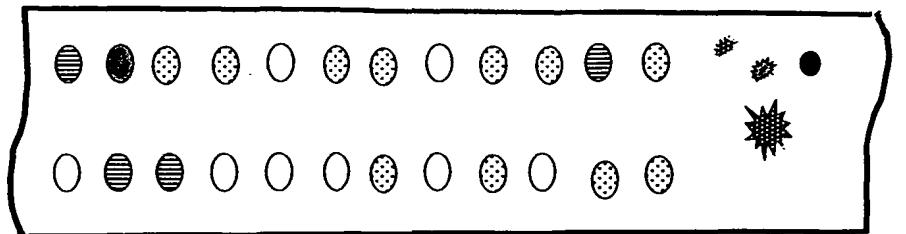
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(54) Title: BIOMARKER PANEL FOR COLORECTAL CANCER

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(57) Abstract: A panel of biomarkers has been identified for analysis of colorectal cancer. The panel, originally identified using a mouse colon cancer model, has been used to assess changes in human tissue from surgical and biopsy samples against a normal human control panel of biomarkers. The panel may be used for providing a cost effective, rapid, noninvasive procedure for risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, detecting relapse, and for the discovery of therapeutic intervention of colorectal cancer.

**BIOMARKER PANEL FOR COLORECTAL CANCER****Reference to Related Applications**

5        This application claims priority to U.S. Provisional Patent Application 60/488,660 entitled Molecular Marker Panel for Determination of Colorectal Cancer, by Nancy M. Lee et al., filed July 18, 2003 (Attorney Docket CPMC-01000US0); and U.S. Patent Application 10/690,880 entitled Biomarker Panel for Colorectal Cancer, by Nancy M. Lee et al., filed October 22, 2003  
10      (Attorney Docket CPMC-01000US1), both of which are incorporated herein by reference.

**Background**

15      The field of art of this disclosure concerns biomarkers for colorectal cancer (CRC). These biomarkers are useful for risk assessment, early detection, establishing prognosis, evaluation of intervention, recurrence of CRC, and discovery of therapeutic intervention, and methods of use thereof.

20      In the field of medicine, clinical procedures providing for the risk assessment and early detection of CRC have been long sought. Currently, CRC is the second leading cause of cancer-related deaths in the Western world. One picture that has clearly emerged through decades of research into CRC is that early detection is critical to enhanced survival rates.

25      The currently accepted methods for CRC screening include the fecal occult blood test (FOBT), x-ray using double contrast between barium enema and air (DCBE), sigmoidoscopy, and colonoscopy. Sigmoidoscopy is an invasive procedure that visually examines the lower third of the colon using a lighted, flexible endoscope, while a related method, colonoscopy, is a procedure that examines the entire colon. In both cases, biopsy samples can be taken during the procedure.

30      Concerning the accepted methods for screening, none clearly possess what is desired in a screening examination for CRC. While FOBT is

rapid, it is a very general, and therefore a very non-specific screening method for CRC. Though DCBE has proven useful in specifically imaging abnormalities in the colon, the drawbacks of the DCBE method include: 1.) Patient discomfort in preparation of and during the examination, creating reluctance for compliance of DCBE as a screening method. 2.) Exposure of a patient to x-ray radiation, limiting DCBE in terms of frequency of use as a screening method. 3.) Research indicating that DCBE is more effective in detecting larger growths, which contraindicates its use for early detection. 4.) Biopsy samples cannot be taken during the procedure. 5.) Due to the cost involved, not all insurance providers pay for DCBE screening exams.

Though sigmoidoscopy has gained favor from many physicians, the drawbacks of this method include: 1.) Patient discomfort in preparation of and during the examination, creating reluctance for compliance of sigmoidoscopy as a screening method. 2.) Due to the cost involved, not all insurance providers pay for sigmoidoscopy screening exams. 3.) Since only the lower third of the colon is inspected, there is a suggestion by studies that many significant lesions are in the proximal end of the colon, rendering sigmoidoscopy inadequate. Though colonoscopy addresses the issue of complete inspection of the colon, the drawbacks of colonoscopy as a screening method include: 1.) Creating even more patient discomfort than sigmoidoscopy, therefore generally requiring sedation, and thereby exacerbating the issue with patient compliance. 2.) Due to the cost involved, not all insurance providers pay for colonoscopy screening exams. 3.) There are risks of colonoscopy that include bleeding, and puncture of the lining of the colon.

Emerging spectroscopic technologies, such as magnetic resonance imaging and tomographic imaging each have drawbacks that are drawn from the list of drawbacks for the currently accepted screening methodologies.

Accordingly, there is a need in the art for approaches that have value in early detection and treatment of CRC that are cost effective, rapid, and

minimally or noninvasive. Additional utility would be realized from an approach that would also serve as the basis for establishing prognosis, monitoring patient treatment, and detecting relapse, as well as the discovery of therapeutic intervention of CRC.

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#### Brief Description of Figures

**FIG 1** is a summary of the sequence listings.

**FIGS 2A-2C** show data that illustrate a panel of biomarkers for samples taken from adenomous polyps, and suspect tissues vs. normal controls. **FIGS 2A-2B** are tables that compare the results of model studies done in mouse (2A) for a selection of members of the set of 22 biomarkers listed in the sequence listings with the comparable selection in of biomarkers for human subjects (2B). **FIG 2C** shows the multivariate analysis for 9 markers for 78 biopsies taken from 12 normal patients and 63 biopsies taken from 6 patients with CRC.

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**FIGS 3B-3C** show expression levels for representative biomarkers, IL-8 (3A), CXCR-2 (3B), and COX-2 (3C) for a series of samples taken from a human subject comparing a histologically identified cancerous lesion, a polyp, and an adjacent non-cancerous tissue vs. a normal control.

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**FIGS 4A-4C** show the results of multiple analysis across a 53 cm distance of a colon for a patient with CRC: **4A** shows expression levels for IL-8; **4B** shows expression levels for COX-2; and **4C** shows expression levels for CXCR-2.

#### Detailed Description

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Still another sought after approach apart from currently accepted methods for screening for CRC, has been the search for biomarkers that have value in detection and treatment of CRC. For more than four decades, since the discovery of alpha-fetoprotein (AFP) and carcinogenic embryonic antigen (CEA), the search for biomarkers for cancer detection and treatment in general has been in a state of evolution. Biomarkers for cancer have five potential uses in the management of patient care. Ideally, they would be

used for risk assessment, for early diagnosis, for establishing prognosis, for monitoring treatment, and for detecting relapse. Additionally, such markers could play a valuable role in developing therapeutic interventions.

5 It is further advantageous for the sampling methods used in conjunction with biomarker analysis to be minimally invasive or non-invasive. Examples of such sampling methods include serum, stool, swabs, and the like. Non-invasive and minimally invasive methods increase patient compliance, and generally reduce cost.

10 Clinically, the two criteria that are important for assessing the effectiveness of biomarkers are selectivity and sensitivity. Selectivity of a biomarker defined clinically refers to percentage of patients correctly diagnosed. Sensitivity of a biomarker in a clinical context is defined as the probability that the disease is detected at a curable stage. Ideally, biomarkers would have 100% clinical selectivity and 100% clinical sensitivity. 15 To date, no single biomarker has been identified that has an acceptably high degree of selectivity and sensitivity required to be effective in for the broad range of needs in patient care management. However, from the clinical perspective, single serum biomarkers, such as AFP and CEA have proven to provide value in some aspects of patient care management.

20 For example, elevated serum levels of CEA were first discovered in 1965 in patients with adenocarcinoma of the colon. Elevated levels can be found in a variety of benign and malignant conditions other than colon cancer. Additionally, the production of CEA by early localized tumors of the colon is in the normal range. Therefore CEA lacks both the sensitivity and selectivity required to be of value for risk assessment or early diagnosis. 25 Further, elevated levels of CEA correlate poorly with colon tumor differentiation and stage, rendering CEA as a biomarker for prognosis of colon cancer of limited value. The two areas for which CEA has proven helpful clinically in managing patient care are in evaluating the effectiveness 30 of treatment, and for detecting relapse. Illustrative of this, numerous studies

have found that there is high correlation between elevated serum levels of CEA preceding clinical detection of recurrence of colon cancer. This has proven to be of value in managing the care of high-risk patients with second-look surgical procedures based on rising levels of CEA.

5       Currently, investigations across numerous areas of oncology research, including CRC, ovarian, breast, and head and neck, are finding increased sensitivity and selectivity in panels of markers. It is now generally held that many mutations must take place before normal cell processes are altered, resulting in a disease, such as cancer. Still, given the complexity of  
10      10 biological systems, discovery of panels useful in providing value in patient care management for CRC is in the nascent stage.

15       To date, a greater understanding of the biology of CRC has been gained through the research on adenomous polyposis coli (APC), p53, and Ki-ras genes, as well as the corresponding proteins, and related pathways involved in the regulation thereof. However, there is a distinct difference  
20      15 between research on a specific a gene, its expression, protein product, and regulation, and understanding what genes are critical to include in a panel used to for the analysis of CRC that is useful in the management of patient care for the disease. To date, panels that have been suggested for CRC are comprised of specific point mutations of APC, p53, and Ki-ras, as well as BAT-26, which is a gene that is a microsatellite instability marker.

25       What is disclosed herein is based on studies conducted in mouse multiple intestinal neoplasia (MIN) model, in which expressions levels of genes were screened in adenomous polyps. In the mouse MIN subjects, a chemically induced mutation of the APC gene is effected. The normal control is defined by littermates for which there was no aberration of the APC gene, and are therefore designated wildtype. From studies based on the mouse MIN model, candidate genes were selected for studying human subjects. From these human subject studies, a panel of biomarkers is disclosed  
30      30 herein. Further, what is disclosed are methods for measuring gene and

protein expression levels based on the panel. Additionally, another aspect of what is disclosed are kits which provide the reagents and instructions for measuring gene and protein expression levels based on the panel. The panel, methods and kits are useful in the management of patient care for 5 CRC. Additionally, the panel, methods, and kits are believed useful as the basis for discovery of therapeutic interventions for CRC.

FIG 1 is a table that gives an overview of the sequence listing for the disclosed biomarkers. The combination of biomarkers disclosed forms the basis for monitoring CRC with enhanced selectivity and sensitivity, and 10 therefore providing enhanced management of patient care for CRC. It is to be understood that fragments and variants of the biomarkers described in the sequence listings are also useful biomarkers in a panel used for the analysis of CRC. What is meant by fragment is any incomplete or isolated portion of a polynucleotide or polypeptide in the sequence listing. It is 15 recognized that almost daily, new discoveries are announced for gene variants, particularly for those genes under intense study, such as genes implicated in diseases like cancer. Therefore, the sequence listings given are exemplary of what is now reported for a gene, but it is recognized that for the purpose of an analytical methodology, variants of the gene, and their 20 fragments are also included.

One embodiment of what is disclosed is a panel of biomarkers with the selectivity and sensitivity required for managing patient care for CRC. In Table 1, entries 1-22 are the polynucleotide coding sequences for a panel of biomarkers, and include the name and abbreviation of the gene. Entries 23- 25 44 in Table 1 are the protein, or polypeptide, amino acid sequences that correspond to the coding sequences for entries 1-22. A biomarker, as defined by the National Institutes of Health (NIH) is a molecular indicator of a specific biological property; a biochemical feature or facet that can be used to measure the progress of disease or the effects of treatment. A panel of 30 biomarkers is a selection of biomarkers. Biomarkers may be from a variety of

classes of molecules. As previously mentioned, there is still a need for biomarkers for CRC having the selectivity and sensitivity required to be effective for all aspects of patient care management. Therefore, the selection of an effective set of biomarkers is differentiating in providing the basis for 5 effective determination of CRC.

In another embodiment of this disclosure, expression levels of polynucleotides for the biomarkers indicated in SEQ ID NOs 1-22, are used in the determination of CRC. Such analysis of polynucleotide expression levels is frequently referred to in the art as gene expression profiling. In gene 10 expression profiling, levels of mRNA in a sample are measured as a leading indicator of a biological state, in this case, as an indicator of CRC. One of the most common methods for analyzing gene expression profiling is to create multiple copies from mRNA in a biological sample using a process known as reverse transcription. In the process of reverse transcription, the mRNA from 15 the sample is used to create copies of the corresponding DNA sequence from which the mRNA was originally transcribed. In the reverse transcription amplification process, copies of DNA are created without the regulatory regions in the gene known as introns. These multiple copies made from mRNA are therefore referred to as copy DNA, or cDNA. Entries 45-88 are 20 the sets of primers used in the reverse transcription process for each gene listed in entries 1-22.

Since the reverse transcription procedure amplifies copies of cDNA proportional to the original level of mRNA in a sample, it has become a standard method that allows the analysis of even low levels of mRNA 25 present in a biological sample. Genes may either be up regulated or down regulated in any particular biological state, and hence mRNA levels shift accordingly.

In still another embodiment of this disclosure, expression levels of proteins listed in SEQ ID NOs 23-44, which correspond to the genes 30 indicated in SEQ ID NOs 1-22, are disclosed. The term "polypeptide" or

“polypeptides” is used interchangeably with the term “protein” or “proteins” herein. As discussed previously, proteins have been long investigated for their potential as biomarkers, with limited success. There is value in protein biomarkers as complementary to polynucleotide biomarkers. Reasons for 5 having the information provided by both types of biomarkers include the current observations that mRNA expression levels are not good predictors of protein expression levels, and that mRNA expression levels tell nothing of the post-translational modifications of proteins that are key to their biological activity. Therefore, in order to understand the expression levels of proteins, 10 and their complete structure, the direct analysis of proteins is required.

FIGS 2A-2B show an exemplary panel of biomarkers from the list of 22 biomarkers for which gene expression levels are compared in the mouse MIN model, and in human subjects. The selection for the panel is taken from across the list of the 22 biomarkers and is taken for the purpose of easy 15 visual assimilation of data in order to demonstrate the utility of a panel. Typically, for complex data sets represented in the 22 member panel of biomarkers, multivariate analysis (MANOVA)<sup>6</sup> is applied, such as that demonstrated in FIG 2c.

In FIG 2A, the data reported for the mouse MIN studies represent 20 statistical averaging of a number of animal subjects, and the standard error is reported. The p value on the right indicates the degree of confidence that the values are significantly different. As an example, the first gene listed, SDF-1, is related to the human IL-8 gene, and is in the same super family. For SDF-1, the p value of 0.003 indicates that the probability that the 25 differences in the values of the wildtype control and that of the adenomous polyps of the MIN mice occurred by chance alone is only 3 in 1000. Screening the expression levels in adenomous polyps in the subject mice was specifically targeted, since it has been established that adenomous polyps are useful in risk assessment for CRC. What is demonstrated in FIG

**2A** is that the panel of 6 clearly differentiate the results of the MIN mice over that of the wildtype control.

**FIGS 2B-2C** address the issue of selectivity for biomarker panels.

Regarding biomarkers that have an acceptable level of selectivity for CRC, the incidence of CRC for individuals in families with a history of CRC is 3-4 times that of the general population. However, It is now estimated that 6% of all Americans will develop CRC, and of those 70-80% will occur in people of average risk. There is clearly a need for biomarkers that have the necessary selectivity required for confidence in the determination of CRC.

In **FIG 2B**, the same panel of 6 biomarkers established in the mouse MIN model in **FIG 2A** are the basis for determination of CRC in human subjects. In **FIG 2B**, the results of biopsy tissue determined to be normal by histological evaluation taken from patients known to have CRC are compared to biopsy tissue from individuals validated as normal controls. It should be noted that histological methodologies are the accepted standard for the identification of a cancerous colonic lesion. There are two aspects of **FIG 2B** to further discuss. First, values for gene expression profiling for patient vs. normal control may vary either up, as in the case of IL 8, or down, as in the case of PPAR- $\delta$ . It is the determination of the collective shift for the patient vs. normal control that is significant when using a panel of biomarkers. Second, in glancing through the patient data, sample-to-sample variation can be noted, which is anticipated, given all the patient-to-patient variables. It is clear at a glance that the expression levels for the panel taken as a group distinguish the patient samples overall from the normal control group, even though a value for any one specific biomarker may not in itself distinguish the patient sample from the normal control. For example, the patient designated as H008 has an expression level for PPAR- $\delta$  that is not distinct from the normal control. However, at a glance it is clear that the results of the panel for H008 distinguish it from the normal control set. This demonstrates in principle why a validated panel of markers, given the

complexity and variability of biology, enhance the selectivity of a determination vs. a single marker alone.

**Fig 2c** further serves to emphasize the value of a panel of biomarkers in enhancing the selectivity of a determination between patient vs. normal samples. An example of demonstrating the use of MANOVA for a panel of 9 biomarkers selected from the group of 22 is demonstrated in **Fig 2c**. In this study, 78 sigmoidal-rectal biopsies from 12 normal patients, and 63 sigmoidal-rectal biopsies from non-cancerous sections of 6 patients with sigmoidal-rectal carcinoma were compared. The Wilks' Lambda criterion was used to assess the difference between the patient samples and normal control samples using the 9 biomarkers listed. The lambda value close to 1.0 signifies a significant difference between the patient and normal samples is indicated, with the probability of about 9 chances in 1000 that the difference is by chance alone.

**FIGS 3A-3C and FIGS 4A-4C** address the issue of sensitivity for biomarker panels. As previously mentioned, since survival rates are greatly enhanced with the earliest indication of CRC, biomarkers for risk assessment and early detection of CRC have been long sought. The difference between risk assessment and early detection is the degree of certainty regarding acquiring CRC. Biomarkers that are used for risk assessment confer less than 100% certainty of CRC within a time interval, whereas biomarkers used for early detection confer an almost 100% certainty of the onset of the disease within a specified time interval. Risk factors may be used as surrogate end points for individuals not diagnosed with cancer, providing they there is an established relationship between the surrogate end point and a definitive outcome. An example of an established surrogate end point for CRC is the example of adenomous polyps. What has been established is that the occurrence of adenomous polyps are a necessary, but not sufficient condition for an individual to later develop CRC. This is demonstrated by the fact that 90% percent of all preinvasive

cancerous lesions are adenomous polyps or precursors, but not all individuals with adenomous polyps go on to later develop CRC.

**FIGS 3A-3c** show graphs of gene expression levels taken for multiple biopsy samples taken from the colon of one exemplary patient diagnosed with CRC. The determination of cancerous lesions, polyps, and adjacent tissues was made by conventional histological methods. The expression levels for three of the panel of biomarkers are shown for the biopsy samples categorized in that fashion. Again, as was demonstrated with the examples given in **FIGS 2A-2c**, it is evident that the three markers taken together for the cancerous lesions sampled are significantly different than the normal controls, even though one by itself (CXCR2) would not have been differentiating for this patient. What is additionally indicated in this representation is the distinction between the results of the polyp vs. the normal control. Given that polyps are already accepted as surrogate endpoints for CRC, then a determination of the presence of polyps by a validated analytical methodology using a minimally invasive method, such as a swab, or a non-invasive sampling method, such as a stool sample, would also serve as surrogate end point for risk assessment.

**FIGS 4A-4c** show the results of gene expression levels for three of the biomarkers in biopsy samples taken over a 53 cm region of the colon of a patient with CRC. The irregularly shaped objects represent biopsy samples that were confirmed to be cancerous lesions by histological methodology, while the oval shapes represent samples that were determined to be non-cancerous by histological methodology. Gene expression profiling was done for each of the biopsy samples, as well. The results of the expression profiling, where the legend indicates relative levels in the patient biopsy samples as compared to normal controls, are depicted in **FIGS 4A-4c**.

The representation of **FIGS 4A-4c** indicates the distance over which the biomarkers are able to distinguish differences in the colon tissue for the patient, where these biopsy samples were rendered normal by conventional

histological analysis. These results demonstrate that it is possible to sample cells through a minimally invasive swabbing collection method from an area distant from a cancerous lesion, but capable of indicating a non-normal colon condition. Moreover, collection of a stool sample is an already validated 5 sampling method for collecting sloughed cells or cell debris from which these determinations may be made. In that regard, samples taken either minimally invasively or non-invasively would render samples that could be analyzed using the disclosed panel of biomarkers. Such non-invasive procedures not only reduce the cost of determination of CRC, but reduce the discomfort and 10 risk associated with current methodology. All these factors together increase the attractiveness of regular testing, and hence patient compliance. Increased patient compliance, coupled with an effective determination for CRC, enhance the prospects for early detection, and enhanced survival rates.

15 Methods and kits for the polynucleotide and polypeptide expression profiling for the panel of molecular markers are also contemplated as part of the present disclosure.

20 In one embodiment, a method for gene expression profiling comprises measuring cDNA levels for biomarkers selected in the claimed panel. Such a method requires the use of primers, enzymes, and other reagents for the preparation, detection, and quantitation of cDNAs. The method of creating cDNA from mRNA in a sample is referred to as the reverse transcriptase 25 polymer chain reaction (RT-PCR). The primers listed in SEQ ID NOs 45-88 are particularly suited for use in gene expression profiling using RT-PCR based on the claimed panel. A series of primers were designed using Primer Express Software (Applied Biosystems, Foster City, CA). Specific candidates were chosen, and then tested to verify that only cDNA was amplified, and not contaminated by genomic DNA. The primers listed in SEQ ID NOs 45-88 30 were specifically designed, selected, and tested accordingly. In addition to the primers, reagents such as one including a dinucleotide triphosphate

mixture having all four dinucleotide triphosphates (e.g. dATP, dGTP, dCTP, and dTTP), one having the reverse transcriptase enzyme, and one having a thermostable DNA polymerase are required for RT-PCR. Additionally buffers, inhibitors and activators are also required for the RT-PCR process.

5 Once the cDNA has been sufficiently amplified to a specified end point, the cDNA sample must be prepared for detection and quantitation. Though a number of detection schemes are contemplated, as will be discussed in more detail below, one method contemplated for detection of polynucleotides is fluorescence spectroscopy, and therefore chromophores

10 that are suited to fluorescence spectroscopy are desirable for labeling polynucleotides. One example of such a fluorescent label is SYBR Green, though numerous related chromophores exist, and are known in the art.

In another embodiment, a method for protein expression profiling comprises using an antibody panel based on the claimed panel of biomarkers for measuring targeted polypeptide levels from a biological sample. In one embodiment contemplated for the method, the antibodies for the panel are bound to a solid support. The method for protein expression profiling may use a second antibody having specificity to some portion of the bound polypeptide. Such a second antibody may be labeled with molecules useful for detection and quantitation of the bound polypeptides, and therefore in binding to the polypeptide label it for detection and quantitation. Additionally, other reagents are contemplated for labeling the bound polypeptides for detection and quantitation. Such reagents may either directly label the bound polypeptide or, analogous to a second antibody, may be a moiety with specificity for the bound polypeptide having labels.

15 Examples of such moieties include but are not limited to small molecules such as cofactors, substrates, complexing agents, and the like, or large molecules, such as lectins, peptides, oligonucleotides, and the like. Such moieties may be either naturally occurring or synthetic.

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30 Examples of detection modes contemplated for the disclosed

methods include, but are not limited to spectroscopic techniques, such as fluorescence and UV-Vis spectroscopy, scintillation counting, and mass spectroscopy. Complementary to these modes of detection, examples of labels for the purpose of detection and quantitation used in these methods 5 include, but are not limited to chromophoric labels, scintillation labels, and mass labels. The expression levels of polynucleotides and polypeptides measured using these methods may be normalized to a control established for the purpose of the targeted determination. These methods are believed useful in providing determinations as the basis of effective management of 10 patient care for CRC. These methods may also be used in the discovery of therapeutic interventions for CRC. Additionally, not only biopsy samples from sigmoidoscopy, colonoscopy, or surgery may be analyzed by these methods, but biological samples from non-invasive or minimally invasive collection methods are indicated for these methods, as well.

15 It is further contemplated in what is disclosed to provide kits having the reagents and procedures that facilitate the ready implementation of the methods, and provide consistency and quality control thereby.

In one embodiment, a kit for gene expression profiling comprises the reagents and instructions necessary for the gene expression profiling of the 20 claimed panel. Thus, for example, the reagents may include primers, enzymes, and other reagents for the preparation, detection, and quantitation of cDNAs for the claimed panel of biomarkers. As discussed above, the method of creating cDNA from mRNA in a sample is referred to as the reverse transcriptase polymer chain reaction (RT-PCR). The primers listed in 25 SEQ ID NOs 45-88 are particularly suited for use in gene expression profiling using RT-PCR based on the claimed panel. The primers listed in SEQ ID NOs 45-88 were specifically designed, selected, and tested accordingly. In addition to the primers, reagents such as one including a dinucleotide triphosphate mixture having all four dinucleotide triphosphates 30 (e.g. dATP, dGTP, dCTP, and dTTP), one having the reverse transcriptase

enzyme, and one having a thermostable DNA polymerase are required for RT-PCR. Additionally buffers, inhibitors and activators used for the RT-PCR process are suitable reagents for inclusion in the kit embodiment. Once the cDNA has been sufficiently amplified to a specified end point, the cDNA 5 sample must be prepared for detection and quantitation. One method contemplated for detection of polynucleotides is fluorescence spectroscopy, and therefore chromophores that are suited to fluorescence spectroscopy are desirable for labeling polynucleotides and may also be included in reagents of the kit embodiment. Instructions included with the kit 10 embodiment for gene expression profiling preferably teach the user the following steps: to obtain a biological sample; to isolate cellular RNA from the sample; to amplify copies of cDNA from the sample for each biomarker in the panel, and the panel for which the reagents are provided; and to quantify levels of cDNA amplified from the sample. Though tissue samples from a 15 variety of procedures may be used, the instructions for obtaining a biological sample are preferably whereby the user obtains a sample of colorectal cells in a minimally invasive manner, such as by use of a swab or collection of a stool sample. The instructions may also preferably include the step of comparing the cDNA levels quantified to a control.

20 In another embodiment, a kit for protein expression profiling comprises the reagents and instructions necessary for protein expression profiling of the claimed panel. Thus, in this embodiment, the kit for protein expression profiling includes supplying an antibody panel based on the claimed panel of biomarkers for measuring targeted polypeptide levels from 25 a biological sample. One embodiment contemplated for such a panel includes the antibody panel bound to a solid support. Additionally, the reagents included with the kit for protein expression profiling may use a second antibody having specificity to some portion of the bound polypeptide. Such a second antibody may be labeled with molecules useful for detection 30 and quantitation of the bound polypeptides, and therefore in binding to the

polypeptide label it for detection and quantitation. Additionally, other reagents are contemplated for labeling the bound polypeptides for detection and quantitation. Such reagents may either directly label the bound polypeptide or, analogous to a second antibody, may be a moiety with 5 specificity for the bound polypeptide having labels. Examples of such moieties include but are not limited to small molecules such as cofactors, substrates, complexing agents, and the like, or large molecules, such as lectins, peptides, oligonucleotides, and the like. Such moieties may be either naturally occurring or synthetic. Instructions for the protein expression 10 profiling kit preferably teach the user: to obtain a biological sample; to use the antibody panel supplied with the kit for each biomarker in the panel to bind the polypeptides from the sample; and to quantify levels of polypeptides bound from the sample to the antibody panel. Preferably, the kit instructions also include a step of comparing the polypeptide levels to a control. 15 Preferably the biological sample is obtained by a minimally invasive procedure such as use of a swab to through a stool sample.

Additionally, consumable labware required for sample collection, preparation, and analysis may be provided with the kits.

What has been disclosed herein has been provided for the purposes 20 of illustration and description. It is not intended to be exhaustive or to limit what is disclosed to the precise forms described. Many modifications and variations will be apparent to the practitioner skilled in the art. What is disclosed was chosen and described in order to best explain the principles and practical application of the disclosed embodiments of the art described, 25 thereby enabling others skilled in the art to understand the various embodiments and various modifications that are suited to the particular use contemplated. It is intended that the scope of what is disclosed be defined by the following claims and their equivalence.

**What Is Claimed:**

1. A panel of biomarkers for colorectal cancer and colorectal polyps comprising at least two polynucleotides selected from SEQ ID NOS 1-5.
2. The panel of claim 1, where the panel is selected for analysis of polynucleotide expression levels for colorectal cancer and colorectal polyps.
3. The panel of claim 2, where the polynucleotide expression levels are mRNAs.
4. The panel of claim 2, where the polynucleotide expression levels are cDNAs.
5. The panel of claim 1, where at least one of the polynucleotides is a fragment.
6. The panel of claim 1, where at least one of the polynucleotides is a variant.
7. The panel of claim 1, where the panel is used for the management of patient care in colorectal cancer and colorectal polyps.
8. The panel of claim 7, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.
9. The panel of claim 1, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

10. A panel of biomarkers for colorectal cancer and colorectal polyps comprising:
  - at least two polynucleotides selected from SEQ ID NOs 1-5; and
  - at least one polynucleotide selected from SEQ ID NOs 6-14
11. The panel of claim 10, where the panel is selected for analysis of polynucleotide expression levels for colorectal cancer and colorectal polyps.
12. The panel of claim 11, where the polynucleotide expression levels are mRNAs.
13. The panel of claim 11, where the polynucleotide expression levels are cDNAs.
14. The panel of claim 10, where at least one of the polynucleotides is a fragment.
15. The panel of claim 10, where at least one of the polynucleotides is a variant.
16. The panel of claim 10, where the panel is used in the management of patient care for colorectal cancer and colorectal polyps.
17. The panel of claim 16, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.
18. The panel of claim 10, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.

19. A panel of biomarkers for colorectal cancer and colorectal polyps comprising:
  - at least two polynucleotides selected from SEQ ID NOs 1-5;
  - at least one polynucleotide selected from SEQ ID NOs 6-14; and
  - at least one polynucleotide selected from SEQ ID NOs 15-22.
20. The panel of claim 19, where the panel is selected for analysis of polynucleotide expression levels for colorectal cancer and colorectal polyps.
21. The panel of claim 20, where the polynucleotide expression levels are mRNAs.
22. The panel of claim 20, where the polynucleotide expression levels are cDNAs.
23. The panel of claim 19, where at least one of the polynucleotides is a fragment.
24. The panel of claim 19, where at least one of the polynucleotides is a variant.
25. The panel of claim 25, where the panel is the basis for management of patient care in colorectal cancer and colorectal polyps.
26. The panel of claim 19, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

27. The panel of claim 25, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.
28. A panel of biomarkers for colorectal cancer and colorectal polyps comprising at least two polypeptides selected from SEQ ID NOs 23-27.
29. The panel of claim 28, where the panel is selected for analysis of polypeptide expression levels for colorectal cancer and colorectal polyps.
30. The panel of claim 28, where at least one of the polypeptides is a fragment.
31. The panel of claim 28, where at least one of the polypeptides is a variant.
32. The panel of claim 28, where the panel is used in the management of patient care in colorectal cancer and colorectal polyps.
33. The panel of claim 32, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.
34. The panel of claim 28, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.
35. A panel of biomarkers for colorectal cancer and colorectal polyps comprising:
  - at least two polypeptides selected from SEQ ID NOs 23-27; and
  - at least one polypeptide selected from SEQ ID NOs 28-36.

36. The panel of claim 35, where the panel is selected for analysis of polypeptide expression levels for colorectal cancer and colorectal polyps.
37. The panel of claim 35, where at least one of the polypeptides is a fragment.
38. The panel of claim 35, where at least one of the polypeptides is a variant.
39. The panel of claim 35, where the panel is used in the management of patient care in colorectal cancer and colorectal polyps.
40. The panel of claim 39, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.
41. The panel of claim 35, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.
42. A panel of biomarkers for colorectal cancer and colorectal polyps comprising:
  - at least two polypeptides selected from SEQ ID NOs 23-27;
  - at least one polypeptide selected from SEQ ID NOs 28-36; and
  - at least one polypeptide selected from SEQ ID NOs 37-44.
43. The panel of claim 42, where the panel is selected for analysis of polypeptide expression levels for colorectal cancer and colorectal polyps.

44. The panel of claim 42, where at least one of the polypeptides is a fragment.
45. The panel of claim 42, where at least one of the polypeptides is a variant.
46. The panel of claim 42, where the panel is used in the management of patient care in colorectal cancer and colorectal polyps.
47. The panel of claim 46, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.
48. The panel of claim 42, where the panel is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.
49. A method for measuring expression levels of polynucleotides from biomarkers for colorectal cancer and colorectal polyps, comprising:
  - selecting a panel of biomarkers comprising at least two polynucleotides from SEQ ID NOs 1-5;
  - obtaining a biological sample;
  - isolating cellular RNA from the sample;
  - amplifying copies of cDNA from the sample for each biomarker in the panel; and
  - quantifying levels of cDNA amplified from the sample.
50. The method of claim 49, where the step of selecting a panel of biomarkers further comprises at least one polynucleotide from SEQ ID NOs 6-14.

51. The method of claim 49, where the step of selecting a panel of biomarkers further comprises:
  - at least one polynucleotide from SEQ ID NOs 6-14; and
  - at least one polynucleotide from SEQ ID NOs 15-22.
52. The method of claim 49, where the step of amplifying copies of cDNA further comprises at least two sets of primers chosen from SEQ. ID NOs 45-50.
53. The method of claim 52, where the step of amplifying copies of cDNA further comprises using enzymes and reagents for the preparation of cDNAs.
54. The method of claim 49, where the step of quantifying the levels of cDNA further comprises labeling cDNA.
55. The method of claim 54, where labeling cDNA includes at least one chromophore.
56. The method of claim 49, where the cDNA levels for the sample are compared to a control.
57. The method of claim 56, where the comparison is used in the management of patient care in colorectal cancer and colorectal polyps.
58. The method of claim 57, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.

59. The method of claim 56, where the comparison is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.
60. The method of claim 49, where the step of obtaining a biological sample is by obtaining a sample of colorectal cells.
61. The method of claim 60, where the step of obtaining a sample of colorectal cells is minimally invasive.
62. The method of claim 61, where the minimally invasive step is by use of a swab.
63. The method of claim 60, where the step of obtaining a sample of colorectal cells is non-invasive.
64. The method of claim 63, where the non-invasive step is by collection of a stool sample.
65. A method for measuring expression levels of polypeptides from biomarkers for colorectal cancer and colorectal cancer, comprising:
  - selecting a panel of biomarkers comprising at least two polypeptides from SEQ ID NOs 23-27;
  - obtaining a biological sample;
  - creating an antibody panel for each biomarker in the panel;
  - using the antibody panel to bind the polypeptides from the sample;
  - and
  - quantifying levels of polypeptides bound from the sample to the antibody panel.

66. The method of claim 65, where the step of selecting a panel of biomarkers further comprises at least one polypeptide from SEQ ID NOs 28-36.
67. The method of claim 65, where the step of selecting a panel of biomarkers further comprises:
  - at least one polypeptide from SEQ ID NOs 28-36; and
  - at least one polypeptide from SEQ ID NOs 37-44.
68. The method of claim 65, where the polypeptide levels for the sample are compared to a control.
69. The method of claim 68, where the comparison is used in the management of patient care in colorectal cancer and colorectal polyps.
70. The method of claim 69, where the management of patient care includes one or more of risk assessment, early diagnosis, establishing prognosis, monitoring patient treatment, and detecting relapse.
71. The method of claim 68, where the comparison is used in discovery of therapeutic intervention of colorectal cancer and colorectal polyps.
72. The method of claim 65, where the step of obtaining a biological sample is by obtaining a sample of colorectal cells.
73. The method of claim 72, where the step of obtaining a sample of colorectal cells is minimally invasive.

74. The method of claim 73, where the minimally invasive step is by use of a swab.

75. The method of claim 72, where the step of obtaining a sample of colorectal cells is non-invasive.

76. The method of claim 75, where the non-invasive step is by collection of a stool sample.

77. The method of claim 65, where the step of quantifying the bound polypeptides further comprises labeling the polypeptides.

78. The method of claim 77, where labeling the polypeptides comprises using a second antibody.

79. A kit for the determination of colorectal cancer and colorectal polyps comprising:

at least one reagent that is used in analysis of polynucleotide expression levels for a panel of biomarkers for colorectal cancer and colorectal polyps, where the panel comprises at least two polynucleotides listed in SEQ ID NOs 1-5; and

instructions for using the kit for analyzing the expression levels.

80. The kit of claim 79, where the panel of biomarkers further comprises at least one polynucleotides listed in SEQ ID NOs 6-14.

81. The kit of claim 79, where the panel of biomarkers further comprises:  
at least one polynucleotide selected from SEQ ID NOs 6-14; and  
at least one polynucleotide selected from SEQ ID NOs 15-22.

82. The kit of claim 79, where the polynucleotide expression levels are mRNAs.
83. The kit of claim 79, where the polynucleotide expression levels are cDNAs.
84. The kit of claim 83, where the reagent comprises at least two sets of primers chosen from SEQ. ID NOs 45-50.
85. The kit of claim 84, further comprising reagents for the preparation of cDNA.
86. The kit of claim 79, comprising a reagent that is used for detection and quantitation of polynucleotides.
87. The kit of claim 86, where the reagent includes at least one chromophore.
88. The kit of claim 79, further comprising consumable labware for at least one of sample collection, sample preparation, and sample analysis.
89. A kit for the determination of colorectal cancer and colorectal polyps comprising:
  - at least one reagent used in that analysis of polypeptide expression levels for a panel of biomarkers for colorectal cancer and colorectal polyps, where the panel comprises at least two polypeptides listed in SEQ. ID NOs 23-27; and
  - instructions for using the kit for analyzing the expression levels.

90. The kit of claim 89, where the panel of biomarkers further comprises at least one polynucleotides listed in SEQ ID NOs 28-36.
91. The kit of claim 89, where the panel of biomarkers further comprises: at least one polynucleotide selected from SEQ ID NOs 28-36; and at least one polynucleotide selected from SEQ ID NOs 37-44.
92. The kit of claim 89, where the reagent is an antibody reagent that binds a polypeptide selected in the panel.
93. The kit of claim 89, further comprising a reagent that is used for detection and quantitation of a bound polypeptide.
94. The kit of claim 93, where the reagent includes a second antibody.
95. The kit of claim 89, further comprising consumable labware for at least one of sample collection, sample preparation, and sample analysis.

Sequence ID No. / ID	NCBI Entrez Database	Name	Abbreviation
1. Coding sequence	XM_031289	Interleukin 8	IL8
2. Coding sequence	XM_051900	Prostaglandin endoperoxide synthase 2	PTGS2
3. Coding sequence	M94582	Interleukin 8 receptor B	ILR8RB
4. Coding sequence	NM_005555	Lipocalin 2	LCN2
5. Coding sequence	NM_000331	Serum amyloid A1	SAA1
6. Coding sequence	NM_000757	Macrophage colony stimulating factor 1	CSF1 (MCSF1)
7. Coding sequence	X54489	Melanoma growth stimulatory activity	MGSA
8. Coding sequence	NM_002090	Chemokine (C-X-C motif) ligand 3	CXCL3
9. Coding sequence	NM_032429	Secreted phosphoprotein 1	SPP1 (OPN)
10. Coding sequence	M64349	Cyclin D	CCND1
11. Coding sequence	AX057136	c-Myc	c-Myc
12. Coding sequence	L25610	Cyclin-dependent kinase inhibitor	HUMCDK1
13. Coding sequence	BC021998	Cyclin-dependent kinase inhibitor 2A	CDKN2A
14. Coding sequence	NM_058195	Alternative reading frame p14	CDKN2A
15. Coding sequence	NM_005036	Peroxisome proliferative activated receptor, alpha	PPARA
16. Coding sequence	NM_003059	Peroxisome proliferative activated receptor, gamma	PPARG
17. Coding sequence	NM_006238	Peroxisome proliferative activated receptor, delta	PPARD
18. Coding sequence	NM_030326	CD44 antigen	CD44
19. Coding sequence	NM_044882	Prostaglandin-endoperoxide synthase 1	PTGS1
20. Coding sequence	NM_002131	High-mobility group AT-hook 1 isoform B	HMGA1
21. Coding sequence	X54942	CKS1H2	CKS1H2
22. Coding sequence	U22055	100 kDa coactivator	p100 coactivator
23. Protein	XP_031289	Interleukin 8	IL8
24. Protein	XP_051900	Prostaglandin-endoperoxide synthase 2	COX2
25. Protein	AAA36108	Interleukin 8 receptor B	CXCR2
26. Protein	NP_005555	Lipocalin 2	LCN2
27. Protein	NP_000331	Serum amyloid A1	SAA1
28. Protein	NP_000757	Macrophage colony stimulating factor 1	CSF1 (MCSF1)
29. Protein	CAA38361	Melanoma growth stimulatory activity	Groα
30. Protein	NM_002090	Chemokine (C-X-C motif) ligand 3	CXCL3

Sequence ID No. / ID	NCBI Entrez Database	Name	Abbreviation
31. Protein	XP_032429	Osteopontin	OPN
32. Protein	AAA52136	Cyclin D	cyclin D1
33. Protein	CAC22425	c-Myc	c-Myc
34. Protein	AAA16109	Cyclin-dependent kinase inhibitor 2A	p21
35. Protein	AAH21998	Cyclin-dependent kinase inhibitor 2A	p16
36. Protein	NP_047862	Alternative reading frame p14	p14ARF
37. Protein	NP_005027	Peroxisome proliferative activated receptor, alpha	PPAR $\alpha$
38. Protein	XP_003059	Peroxisome proliferative activated receptor, gamma	PPAR $\gamma$
39. Protein	NP_006229	Peroxisome proliferative activated receptor, delta	PPAR $\delta$
40. Protein	XP_030326	CD44 antigen	CD44
41. Protein	XP_044882	Prostaglandin-endoperoxide synthase 1	COX1
42. Protein	NP_002122	High-mobility group AT-hook 1 isoform B	HYGY1
43. Protein	CAA38703	CKS1 protein homolog	CKS1
44. Protein	AAA80488	100 kDa coactivator	p100 coactivator
45. Forward primer		Interleukin 8	IL8
46. Reverse primer			
47. Forward primer		Prostaglandin-endoperoxide synthase 2	PTGS2
48. Reverse primer			
49. Forward primer		Interleukin 8 receptor B	ILR8RB
50. Reverse primer			
51. Forward primer		Lipocalin 2	LCN2
52. Reverse primer			
53. Forward primer		Serum amyloid A1	SAA1
54. Reverse primer			
55. Forward primer		Macrophage colony stimulating factor 1	CSF1 (MCSF1)
56. Reverse primer			
57. Forward primer		Melanoma growth stimulatory activity	MGSA
58. Reverse primer			
59. Forward primer		Chemokine (C-X-C motif) ligand 3	MGSA
60. Reverse primer			

Sequence ID No. / ID	NCBI Entrez Database	Name	Abbreviation
61. Forward primer		Secreted phosphoprotein 1	SPP1 (OPN)
62. Reverse primer			
63. Forward primer		Cyclin D	CCND1
64. Reverse primer			
65. Forward primer		c-Myc	
66. Reverse primer			
67. Forward primer		Cyclin-dependent kinase inhibitor	HUMCDK1
68. Reverse primer			
69. Forward primer		Cyclin-dependent kinase inhibitor 2A	CDKN2A
70. Reverse primer			
71. Forward primer		Alternative reading frame p14	CDKN2A
72. Reverse primer			
73. Forward primer		Peroxisome proliferative activated receptor, alpha	PPAR $\alpha$
74. Reverse primer			
75. Forward primer		Peroxisome proliferative activated receptor, gamma	PPAR $\gamma$
76. Reverse primer			
77. Forward primer		Peroxisome proliferative activated receptor, delta	PPAR $\delta$
78. Reverse primer			
79. Forward primer		CD44 antigen	CD44
80. Reverse primer			
81. Forward primer		Prostaglandin-endoperoxide synthase 1	COX1
82. Reverse primer			
83. Forward primer		High-mobility group AT-hook 1 isoform B	HMGY1
84. Reverse primer			
85. Forward primer		CKS1 protein homolog	CKS1
86. Reverse primer			
87. Forward primer		100 kDa coactivator	p100 coactivator
88. Reverse primer			

Relative Gene Expression Levels in Colon Polyps (Average  $\pm$  SE)

No.	Genes	Wild-Type Littermate	Individual Poly	P Value
1	SDF-1	1.23 $\pm$ 0.34	11.02 $\pm$ 2.45	0.003
2	COX2	1.41 $\pm$ 0.25	87.48 $\pm$ 16.50	<0.001
3	CXCR2	1.41 $\pm$ 0.35	11221 $\pm$ 23.76	<0.001
4	OPN	1.62 $\pm$ 0.60	463.37 $\pm$ 130.49	0.004
5	MCSF1	1.05 $\pm$ 0.15	4.26 $\pm$ 1.60	0.08
6	PPAR $\delta$	1.16 $\pm$ 0.27	0.44 $\pm$ 0.05	0.04

FIG. 2A

## Relative Gene Expressions in Normal-Appearing Mucosa from Colon Cancer

	Sigmoid and Rectum					Ascending Colon				
	NB	H002	H004	H006	H008	H011	NB	H003	H009	H010
IL-8	1.80 $\pm$ 0.26	28.91	7.14	6.88	18.35	24.67	1.72 $\pm$ 0.35	16.03	4.90	28.26
COX2	1.85 $\pm$ 0.29	13.54	10.34	18.23	14.63	1.87	1.74 $\pm$ 0.45	25.48	11.98	33.06
CXCR2	1.31 $\pm$ 0.14	11.35	6.82	6.85	7.18	100.20	1.26 $\pm$ 0.17	10.23	22.62	11.20
OPN	2.11 $\pm$ 0.52	10.85	9.84	11.88	21.29	3.41	1.43 $\pm$ 0.20	26.83	23.97	64.13
MCSF1	1.69 $\pm$ 0.19	4.49	11.88	12.84	7.24	7.98	1.57 $\pm$ 0.22	12.40	17.89	14.97
PPAR- $\delta$	1.14 $\pm$ 0.07	0.10	0.09	0.12	1.28	0.96	1.16 $\pm$ 0.11	0.09	1.10	0.30

FIG. 2B

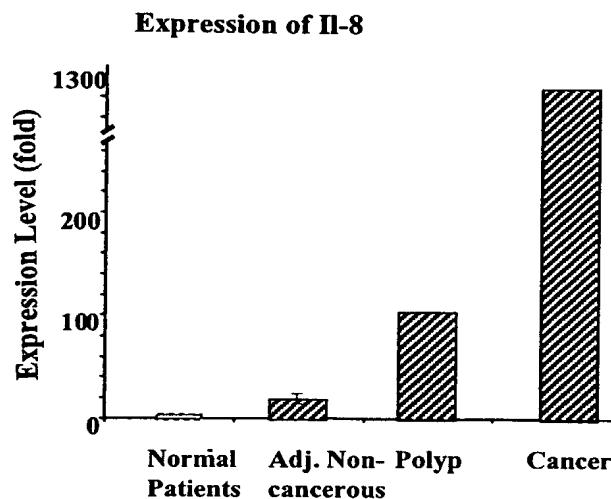
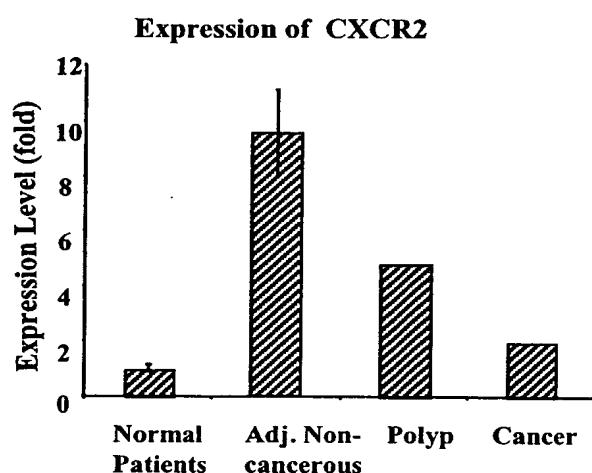
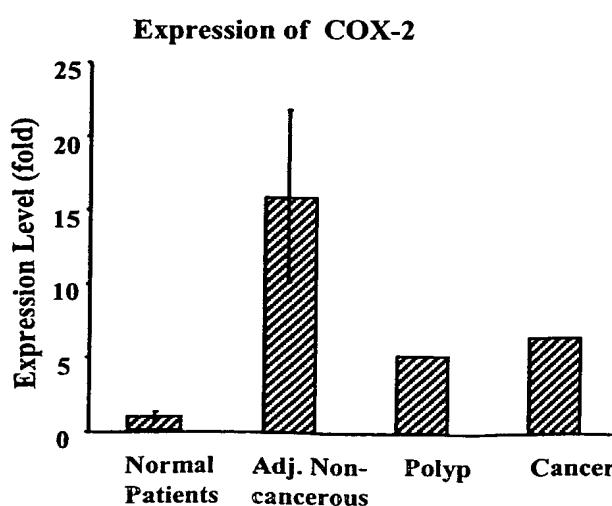
Dependent Variable: IL-8, M-CSF-1, COX-2, OPN, p21, PPAR- $\gamma$ , CXCR2, CD44, PPAR- $\delta$

Results for Multivariate Analysis: Wilks Lambda Criterion

Source	Lambda	probability
Cancer	0.989	0.0086

FIG. 2C

5/6

**Fig. 3A****Fig. 3B****Fig. 3C**

IL-8

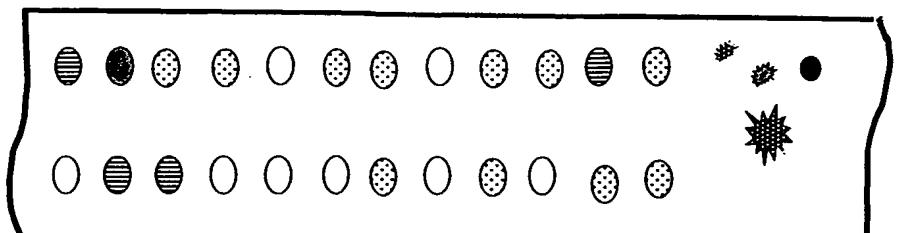


Fig. 4A

COX2

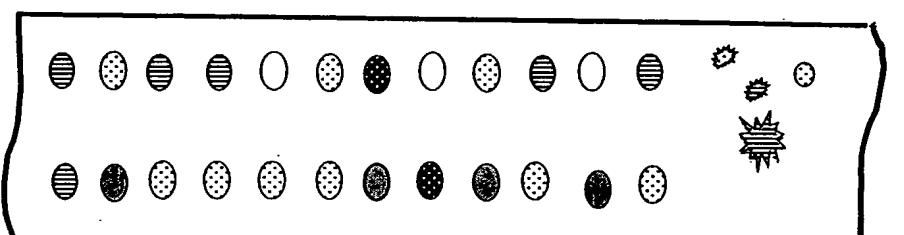


Fig. 4B

CXCR2

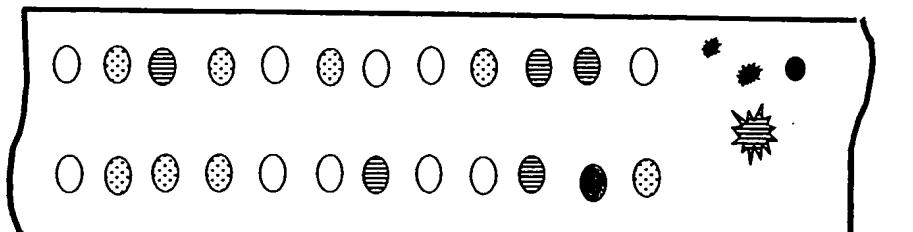


Fig. 4C

## SEQUENCE LISTING

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2/88

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4/88

cgc ctt ttc aag gat gga aaa atg aaa tat cag ata att gat gga gag	835																																																																																																										
Arg Leu Phe Lys Asp Gly Lys Met Lys Tyr Gln Ile Ile Asp Gly Glu																																																																																																											
235	240	245		atg tat cct ccc aca gtc aaa gat act cag gca gag atg atc tac cct	883	Met Tyr Pro Pro Thr Val Lys Asp Thr Gln Ala Glu Met Ile Tyr Pro		250	255	260		cct caa gtc cct gag cat cta cgg ttt gct gtg ggg cag gag gtc ttt	931	Pro Gln Val Pro Glu His Leu Arg Phe Ala Val Gly Gln Glu Val Phe		265	270	275		ggt ctg gtg cct ggt ctg atg atg tat gcc aca atc tgg ctg cgg gaa	979	Gly Leu Val Pro Gly Leu Met Met Tyr Ala Thr Ile Trp Leu Arg Glu		280	285	290		cac aac aga gta tgc gat gtg ctt aaa cag gag cat cct gaa tgg ggt	1027	His Asn Arg Val Cys Asp Val Leu Lys Gln Glu His Pro Glu Trp Gly		295	300	305	310	gat gag cag ttg ttc cag aca agc agg cta ata ctg ata gga gag act	1075	Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu Ile Leu Ile Gly Glu Thr		315	320	325		att aag att gtg att gaa gat tat gtg caa cac ttg agt ggc tat cac	1123	Ile Lys Ile Val Ile Glu Asp Tyr Val Gln His Leu Ser Gly Tyr His		330	335	340		ttc aaa ctg aaa ttt gac cca gaa cta ctt ttc aac aaa caa ttc cag	1171	Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu Phe Asn Lys Gln Phe Gln		345	350	355		tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat	1219	Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His		360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450	
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250	255	260		cct caa gtc cct gag cat cta cgg ttt gct gtg ggg cag gag gtc ttt	931	Pro Gln Val Pro Glu His Leu Arg Phe Ala Val Gly Gln Glu Val Phe		265	270	275		ggt ctg gtg cct ggt ctg atg atg tat gcc aca atc tgg ctg cgg gaa	979	Gly Leu Val Pro Gly Leu Met Met Tyr Ala Thr Ile Trp Leu Arg Glu		280	285	290		cac aac aga gta tgc gat gtg ctt aaa cag gag cat cct gaa tgg ggt	1027	His Asn Arg Val Cys Asp Val Leu Lys Gln Glu His Pro Glu Trp Gly		295	300	305	310	gat gag cag ttg ttc cag aca agc agg cta ata ctg ata gga gag act	1075	Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu Ile Leu Ile Gly Glu Thr		315	320	325		att aag att gtg att gaa gat tat gtg caa cac ttg agt ggc tat cac	1123	Ile Lys Ile Val Ile Glu Asp Tyr Val Gln His Leu Ser Gly Tyr His		330	335	340		ttc aaa ctg aaa ttt gac cca gaa cta ctt ttc aac aaa caa ttc cag	1171	Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu Phe Asn Lys Gln Phe Gln		345	350	355		tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat	1219	Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His		360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450									
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265	270	275		ggt ctg gtg cct ggt ctg atg atg tat gcc aca atc tgg ctg cgg gaa	979	Gly Leu Val Pro Gly Leu Met Met Tyr Ala Thr Ile Trp Leu Arg Glu		280	285	290		cac aac aga gta tgc gat gtg ctt aaa cag gag cat cct gaa tgg ggt	1027	His Asn Arg Val Cys Asp Val Leu Lys Gln Glu His Pro Glu Trp Gly		295	300	305	310	gat gag cag ttg ttc cag aca agc agg cta ata ctg ata gga gag act	1075	Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu Ile Leu Ile Gly Glu Thr		315	320	325		att aag att gtg att gaa gat tat gtg caa cac ttg agt ggc tat cac	1123	Ile Lys Ile Val Ile Glu Asp Tyr Val Gln His Leu Ser Gly Tyr His		330	335	340		ttc aaa ctg aaa ttt gac cca gaa cta ctt ttc aac aaa caa ttc cag	1171	Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu Phe Asn Lys Gln Phe Gln		345	350	355		tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat	1219	Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His		360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																	
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280	285	290		cac aac aga gta tgc gat gtg ctt aaa cag gag cat cct gaa tgg ggt	1027	His Asn Arg Val Cys Asp Val Leu Lys Gln Glu His Pro Glu Trp Gly		295	300	305	310	gat gag cag ttg ttc cag aca agc agg cta ata ctg ata gga gag act	1075	Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu Ile Leu Ile Gly Glu Thr		315	320	325		att aag att gtg att gaa gat tat gtg caa cac ttg agt ggc tat cac	1123	Ile Lys Ile Val Ile Glu Asp Tyr Val Gln His Leu Ser Gly Tyr His		330	335	340		ttc aaa ctg aaa ttt gac cca gaa cta ctt ttc aac aaa caa ttc cag	1171	Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu Phe Asn Lys Gln Phe Gln		345	350	355		tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat	1219	Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His		360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																									
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295	300	305	310	gat gag cag ttg ttc cag aca agc agg cta ata ctg ata gga gag act	1075	Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu Ile Leu Ile Gly Glu Thr		315	320	325		att aag att gtg att gaa gat tat gtg caa cac ttg agt ggc tat cac	1123	Ile Lys Ile Val Ile Glu Asp Tyr Val Gln His Leu Ser Gly Tyr His		330	335	340		ttc aaa ctg aaa ttt gac cca gaa cta ctt ttc aac aaa caa ttc cag	1171	Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu Phe Asn Lys Gln Phe Gln		345	350	355		tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat	1219	Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His		360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																	
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315	320	325		att aag att gtg att gaa gat tat gtg caa cac ttg agt ggc tat cac	1123	Ile Lys Ile Val Ile Glu Asp Tyr Val Gln His Leu Ser Gly Tyr His		330	335	340		ttc aaa ctg aaa ttt gac cca gaa cta ctt ttc aac aaa caa ttc cag	1171	Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu Phe Asn Lys Gln Phe Gln		345	350	355		tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat	1219	Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His		360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																									
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330	335	340		ttc aaa ctg aaa ttt gac cca gaa cta ctt ttc aac aaa caa ttc cag	1171	Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu Phe Asn Lys Gln Phe Gln		345	350	355		tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat	1219	Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His		360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																																	
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345	350	355		tac caa aat cgt att gct gct gaa ttt aac acc ctc tat cac tgg cat	1219	Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn Thr Leu Tyr His Trp His		360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																																									
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360	365	370		ccc ctt ctg cct gac acc ttt caa att cat gac cag aaa tac aac tat	1267	Pro Leu Leu Pro Asp Thr Phe Gln Ile His Asp Gln Lys Tyr Asn Tyr		375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																																																	
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375	380	385	390	caa cag ttt atc tac aac aac tct ata ttg ctg gaa cat gga att acc	1315	Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu Leu Glu His Gly Ile Thr		395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																																																									
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395	400	405		cag ttt gtt gaa tca ttc acc agg caa att gct ggc agg gtt gct ggt	1363	Gln Phe Val Glu Ser Phe Thr Arg Gln Ile Ala Gly Arg Val Ala Gly		410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																																																																	
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410	415	420		ggt agg aat gtt cca ccc gca gta cag aaa gta tca cag gct tcc att	1411	Gly Arg Asn Val Pro Pro Ala Val Gln Lys Val Ser Gln Ala Ser Ile		425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																																																																									
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425	430	435		gac cag agc agg cag atg aaa tac cag tct ttt aat gag tac cgc aaa	1459	Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser Phe Asn Glu Tyr Arg Lys		440	445	450																																																																																																	
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cgc ttt atg ctg aag ccc tat gaa tca ttt gaa gaa ctt aca gga gaa	1507
Arg Phe Met Leu Lys Pro Tyr Glu Ser Phe Glu Glu Leu Thr Gly Glu	
455 460 465 470	
aag gaa atg tct gca gag ttg gaa gca ctc tat ggt gac atc gat gct	1555
Lys Glu Met Ser Ala Glu Leu Glu Ala Leu Tyr Gly Asp Ile Asp Ala	
475 480 485	
gtg gag ctg tat cct gcc ctt ctg gta gaa aag cct cg <sup>g</sup> cca gat gcc	1603
Val Glu Leu Tyr Pro Ala Leu Leu Val Glu Lys Pro Arg Pro Asp Ala	
490 495 500	
atc ttt ggt gaa acc atg gta gaa gtt gga gca cca ttc tcc ttg aaa	1651
Ile Phe Gly Glu Thr Met Val Glu Val Gly Ala Pro Phe Ser Leu Lys	
505 510 515	
gga ctt atg ggt aat gtt ata tgt tct cct gcc tac tgg aag cca agc	1699
Gly Leu Met Gly Asn Val Ile Cys Ser Pro Ala Tyr Trp Lys Pro Ser	
520 525 530	
act ttt ggt gga gaa gtg ggt ttt caa atc atc aac act gcc tca att	1747
Thr Phe Gly Gly Glu Val Gly Phe Gln Ile Ile Asn Thr Ala Ser Ile	
535 540 545 550	
cag tct ctc atc tgc aat aac gtg aag ggc tgt ccc ttt act tca ttc	1795
Gln Ser Leu Ile Cys Asn Asn Val Lys Gly Cys Pro Phe Thr Ser Phe	
555 560 565	
agt gtt cca gat cca gag ctc att aaa aca gtc acc atc aat gca agt	1843
Ser Val Pro Asp Pro Glu Leu Ile Lys Thr Val Thr Ile Asn Ala Ser	
570 575 580	
tct tcc cgc tcc gga cta gat gat atc aat ccc aca gta cta cta aaa	1891
Ser Ser Arg Ser Gly Leu Asp Asp Ile Asn Pro Thr Val Leu Leu Lys	
585 590 595	
gaa cgt tcg act gaa ctg tagaagtcta atgatcatat ttat <sup>tttttttt</sup>	1939
Glu Arg Ser Thr Glu Leu	
600	
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7/88

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Val Val Ile Ile Tyr Ala Leu Val Phe Leu Leu Ser Leu Leu Gly Asn			
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tcc ctc gtg atg ctg gtc atc tta tac agc agg gtc ggc cgc tcc gtc	298		
Ser Leu Val Met Leu Val Ile Leu Tyr Ser Arg Val Gly Arg Ser Val			
70	75	80	
act gat gtc tac ctg ctg aac cta gcc ttg gcc gac cta ctc ttt gcc	346		
Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ala Asp Leu Leu Phe Ala			
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ctg acc ttg ccc atc tgg gcc gcc tcc aag gtg aat ggc tgg att ttt	394		
Leu Thr Leu Pro Ile Trp Ala Ala Ser Lys Val Asn Gly Trp Ile Phe			
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Gly Thr Phe Leu Cys Lys Val Val Ser Leu Leu Lys Glu Val Asn Phe			
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tat agt ggc atc ctg cta ctg gcc tgc atc agt gtg gac cgt tac ctg	490		
Tyr Ser Gly Ile Leu Leu Ala Cys Ile Ser Val Asp Arg Tyr Leu			
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gcc att gtc cat gcc aca cgc aca ctg acc cag aag cgc tac ttg gtc	538		
Ala Ile Val His Ala Thr Arg Thr Leu Thr Gln Lys Arg Tyr Leu Val			
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Lys Phe Ile Cys Leu Ser Ile Trp Gly Leu Ser Leu Leu Ala Leu			
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Pro Val Leu Leu Phe Arg Arg Thr Val Tyr Ser Ser Asn Val Ser Pro			
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gcc tgc tat gag gac atg ggc aac aat aca gca aac tgg cgg atg ctg	682		
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Met Gly Gln Lys His Arg Ala Met Arg Val Ile Phe Ala Val Val Leu			
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8/88

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His Ile Asp Arg Ala Leu Asp Ala Thr Glu Ile Leu Gly Ile Leu His	
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Ser Cys Leu Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys Phe Arg	
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His Gly Leu Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser Lys Asp	
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Ser Leu Pro Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser Ser Gly	
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His Thr Ser Thr Thr Leu	
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1 5 10 15	

9/88

cat gcc cag gcc cag gac tcc acc tca gac ctg atc cca gcc cca cct	96																																																																																												
His Ala Gln Ala Gln Asp Ser Thr Ser Asp Leu Ile Pro Ala Pro Pro																																																																																													
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ggg aag tgg tat gtg gta ggc ctg gca ggg aat gca att ctc aga gaa	192																																																																																												
Gly Lys Trp Tyr Val Val Gly Leu Ala Gly Asn Ala Ile Leu Arg Glu																																																																																													
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gac aaa gac ccg caa aag atg tat gcc acc atc tat gag ctg aaa gaa	240																																																																																												
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Lys Val Ser Gln Asn Arg Glu Tyr Phe Lys Ile Thr Leu Tyr Gly Arg																																																																																													
145	150		155		160	acc aag gag ctg act tcg gaa cta aag gag aac ttc atc cgc ttc tcc	528	Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser		165	170		175	aaa tat ctg ggc ctc cct gaa aac cac atc gtc ttc cct gtc cca atc	576	Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile		180	185		190	gac cag tgt atc gac ggc tga	597	Asp Gln Cys Ile Asp Gly		195																																																																			
	155		160	acc aag gag ctg act tcg gaa cta aag gag aac ttc atc cgc ttc tcc	528	Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser		165	170		175	aaa tat ctg ggc ctc cct gaa aac cac atc gtc ttc cct gtc cca atc	576	Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile		180	185		190	gac cag tgt atc gac ggc tga	597	Asp Gln Cys Ile Asp Gly		195																																																																					
	160																																																																																												
acc aag gag ctg act tcg gaa cta aag gag aac ttc atc cgc ttc tcc	528																																																																																												
Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser																																																																																													
165	170		175	aaa tat ctg ggc ctc cct gaa aac cac atc gtc ttc cct gtc cca atc	576	Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile		180	185		190	gac cag tgt atc gac ggc tga	597	Asp Gln Cys Ile Asp Gly		195																																																																													
	175																																																																																												
aaa tat ctg ggc ctc cct gaa aac cac atc gtc ttc cct gtc cca atc	576																																																																																												
Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile																																																																																													
180	185		190	gac cag tgt atc gac ggc tga	597	Asp Gln Cys Ile Asp Gly		195																																																																																					
	190																																																																																												
gac cag tgt atc gac ggc tga	597																																																																																												
Asp Gln Cys Ile Asp Gly																																																																																													
195																																																																																													

<210> 5  
<211> 369  
<212> DNA  
<213> Homo sapiens

10/88

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<220>
<221> CDS
<222> (1)..(369)

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1 5 10 15

agc agc cga agc ttc ttt tcg ttc ctt ggc gag gct ttt gat ggg gct 96
Ser Ser Arg Ser Phe Phe Ser Phe Leu Gly Glu Ala Phe Asp Gly Ala
20 25 30

cgg gac atg tgg aga gcc tac tct gac atg aga gaa gcc aat tac atc 144
Arg Asp Met Trp Arg Ala Tyr Ser Asp Met Arg Glu Ala Asn Tyr Ile
35 40 45

ggc tca gac aaa tac ttc cat gct cgg ggg aac tat gat gct gcc aaa 192
Gly Ser Asp Lys Tyr Phe His Ala Arg Gly Asn Tyr Asp Ala Ala Lys
50 55 60

agg gga cct ggg ggt gtc tgg gct gca gaa gcg atc agc gat gcc aga 240
Arg Gly Pro Gly Gly Val Trp Ala Ala Glu Ala Ile Ser Asp Ala Arg
65 70 75 80

gag aat atc cag aga ttc ttt ggc cat ggt gcg gag gac tcg ctg gct 288
Glu Asn Ile Gln Arg Phe Phe Gly His Gly Ala Glu Asp Ser Leu Ala
85 90 95

gat cag gct gcc aat gaa tgg ggc agg agt ggc aaa gac ccc aat cac 336
Asp Gln Ala Ala Asn Glu Trp Gly Arg Ser Gly Lys Asp Pro Asn His
100 105 110

ttc cga cct gct ggc ctg cct gag aaa tac tga 369
Phe Arg Pro Ala Gly Leu Pro Glu Lys Tyr
115 120

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<210> 6
<211> 3939
<212> DNA
<213> Homo sapiens

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<222> (106)..(1767)

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gccggggcgc ccactccgca gcagccagcg agccagctgc cccgt atg acc gcg ccg 117
Met Thr Ala Pro
1

ggc gcc gcc ggg cgc tgc cct ccc acg aca tgg ctg ggc tcc ctg ctg 165
Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu Gly Ser Leu Leu
5 10 15 20

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11/88

ttg ttg gtc tgt ctc ctg gcg agc agg agt atc acc gag gag gtg tcg	213
Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr Glu Glu Val Ser	
25 30 35	
gag tac tgt agc cac atg att ggg agt gga cac ctg cag tct ctg cag	261
Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu Gln Ser Leu Gln	
40 45 50	
cg <sup>g</sup> ctg att gac agt cag atg gag acc tcg tgc caa att aca ttt gag	309
Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln Ile Thr Phe Glu	
55 60 65	
ttt gta gac cag gaa cag ttg aaa gat cca gtg tgc tac ctt aag aag	357
Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys Tyr Leu Lys Lys	
70 75 80	
gca ttt ctc ctg gta caa gac ata atg gag gac acc atg cgc ttc aga	405
Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr Met Arg Phe Arg	
85 90 95 100	
gat aac acc gcc aat ccc atc gcc att gtg cag ctg cag gaa ctc tct	453
Asp Asn Thr Ala Asn Pro Ile Ala Ile Val Gln Leu Gln Glu Leu Ser	
105 110 115	
ttg agg ctg aag agc tgc ttc acc aag gat tat gaa gag cat gac aag	501
Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu Glu His Asp Lys	
120 125 130	
gcc tgc gtc cga act ttc tat gag aca cct ctc cag ttg ctg gag aag	549
Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln Leu Leu Glu Lys	
135 140 145	
gtc aag aat gtc ttt aat gaa aca aag aat ctc ctt gac aag gac tgg	597
Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu Asp Lys Asp Trp	
150 155 160	
aat att ttc agc aag aac tgc aac aac agc ttt gct gaa tgc tcc agc	645
Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala Glu Cys Ser Ser	
165 170 175 180	
caa gat gtg gtc acc aag cct gat tgc aac tgc ctg tac ccc aaa gcc	693
Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu Tyr Pro Lys Ala	
185 190 195	
atc cct agc agt gac ccg gcc tct gtc tcc cct cat cag ccc ctc gcc	741
Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His Gln Pro Leu Ala	
200 205 210	
ccc tcc atg gcc cct gtg gct ggc ttg acc tgg gag gac tct gag gga	789
Pro Ser Met Ala Pro Val Ala Gly Leu Thr Trp Glu Asp Ser Glu Gly	
215 220 225	
act gag ggc agc tcc ctc ttg cct ggt gag cag ccc ctg cac aca gtg	837
Thr Glu Gly Ser Ser Leu Leu Pro Gly Glu Gln Pro Leu His Thr Val	
230 235 240	

12/88

gat cca ggc agt gcc aag cag cgg cca ccc agg agc acc tgc cag agc	245	250	255	260	885
Asp Pro Gly Ser Ala Lys Gln Arg Pro Pro Arg Ser Thr Cys Gln Ser					
ttt gag ccg cca gag acc cca gtt gtc aag gac agc acc atc ggt ggc	265	270	275		933
Phe Glu Pro Pro Glu Thr Pro Val Val Lys Asp Ser Thr Ile Gly Gly					
tca cca cag cct cgc ccc tct gtc ggg gcc ttc aac ccc ggg atg gag	280	285	290		981
Ser Pro Gln Pro Arg Pro Ser Val Gly Ala Phe Asn Pro Gly Met Glu					
gat att ctt gac tct gca atg ggc act aat tgg gtc cca gaa gaa gcc	295	300	305		1029
Asp Ile Leu Asp Ser Ala Met Gly Thr Asn Trp Val Pro Glu Glu Ala					
tct gga gag gcc agt gag att ccc gta ccc caa ggg aca gag ctt tcc	310	315	320		1077
Ser Gly Glu Ala Ser Glu Ile Pro Val Pro Gln Gly Thr Glu Leu Ser					
ccc tcc agg cca gga ggg ggc agc atg cag aca gag ccc gcc aga ccc	325	330	335	340	1125
Pro Ser Arg Pro Gly Gly Ser Met Gln Thr Glu Pro Ala Arg Pro					
agc aac ttc ctc tca gca tct tct cca ctc cct gca tca gca aag ggc	345	350	355		1173
Ser Asn Phe Leu Ser Ala Ser Ser Pro Leu Pro Ala Ser Ala Lys Gly					
caa cag ccg gca gat gta act gct aca gcc ttg ccc agg gtg ggc ccc	360	365	370		1221
Gln Gln Pro Ala Asp Val Thr Ala Thr Ala Leu Pro Arg Val Gly Pro					
gtg atg ccc act ggc cag gac tgg aat cac acc ccc cag aag aca gac	375	380	385		1269
Val Met Pro Thr Gly Gln Asp Trp Asn His Thr Pro Gln Lys Thr Asp					
cat cca tct gcc ctg ctc aga gac ccc ccg gag cca ggc tct ccc agg	390	395	400		1317
His Pro Ser Ala Leu Leu Arg Asp Pro Pro Glu Pro Gly Ser Pro Arg					
atc tca tca ctg cgc ccc cag gcc ctc agc aac ccc tcc acc ctc tct	405	410	415	420	1365
Ile Ser Ser Leu Arg Pro Gln Ala Leu Ser Asn Pro Ser Thr Leu Ser					
gct cag cca cag ctt tcc aga agc cac tcc tcg ggc agc gtg ctg ccc	425	430	435		1413
Ala Gln Pro Gln Leu Ser Arg Ser His Ser Ser Gly Ser Val Leu Pro					
ctt ggg gag ctg gag ggc agg agg agc acc agg gat cgg acg agc ccc	440	445	450		1461
Leu Gly Glu Leu Glu Gly Arg Arg Ser Thr Arg Asp Arg Thr Ser Pro					
gca gag cca gaa gca gca cca gca agt gaa ggg gca gcc agg ccc ctg	455	460	465		1509
Ala Glu Pro Glu Ala Ala Pro Ala Ser Glu Gly Ala Ala Arg Pro Leu					

13/88

ccc cgt ttt aac tcc gtt cct ttg act gac aca ggc cat gag agg cag	1557
Pro Arg Phe Asn Ser Val Pro Leu Thr Asp Thr Gly His Glu Arg Gln	
470 475 480	
tcc gag gga tcc tcc agc ccg cag ctc cag gag tct gtc ttc cac ctg	1605
Ser Glu Gly Ser Ser Pro Gln Leu Gln Glu Ser Val Phe His Leu	
485 490 495 500	
ctg gtg ccc agt gtc atc ctg gtc ttg ctg gct gtc gga ggc ctc ttg	1653
Leu Val Pro Ser Val Ile Leu Val Leu Ala Val Gly Gly Leu Leu	
505 510 515	
ttc tac agg tgg agg cgg cgg agc cat caa gag cct cag aga gcg gat	1701
Phe Tyr Arg Trp Arg Arg Ser His Gln Glu Pro Gln Arg Ala Asp	
520 525 530	
tct ccc ttg gag caa cca gag ggc agc ccc ctg act cag gat gac aga	1749
Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr Gln Asp Asp Arg	
535 540 545	
cag gtg gaa ctg cca gtg tagagggaaat tctaagctgg acgcacagaa	1797
Gln Val Glu Leu Pro Val	
550	
cagtccttc gtgggaggag acattatggg gcgtccacca ccaccctcc ctggccatcc	1857
tcctggaatg tggctgccc tccaccagag ctccctgcctg ccaggactgg accagagcag	1917
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aggctggta gccccggctca ggaccctt ccctcagggg ctgcagcctc ctctcactcc	2097
cttccatgcc ggaacccagg ccagggaccc accggcctgt ggtttggaa aaagcagggt	2157
gcacgctgag gagtgaaaca accctgcacc cagagggcct gcctgggcc aaggtatccc	2217
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gaacactgta cctgcctgt gaacagcctc ccccccgtcca tccatgagcc agcatccgtc	2637
cgtcctccac tctccagccct ctccccagcc tccctgcactg agctggcctc accagtcgac	2697
tgagggagcc cctcagccct gaccttctcc tgacctggcc tttgactccc cggagtgag	2757
tgggggtggga gaacctcctg ggccggccagc cagagccgct cttaggctg tggcttcgc	2817

14/88

ccaggtttct gcatcttcca ctttgcatt cccaaaggaa aagggactag tgggagagag 2877  
 caagggaggg gagggcacag acagagagcc tacagggcga gctctgactg aagatgggcc 2937  
 tttgaaatat aggtatgcac ctgaggttgg gggagggtct gcactccaa accccagcgc 2997  
 agtgtccctt ccctgctgcc gacaggaacc tggggctgag caggttatcc ctgtcaggag 3057  
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 acccttctt cctcctgacc ttggtcagca gtatgacact ccaactctca cccacccccc 3177  
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 ctaggcaacg agcgacaggg ctgccagttt cccctgggtt cctttgtgt gctgtgtgcc 3357  
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 ccgtgacttt cccttcctgc ccaggaaagt gagggtcggc tggcccccacc ttccctgtcc 3477  
 tgatgccgac agcttaggaa agggactga acttgcataat ggggcttagc cttctagtc 3537  
 cagcctctat atttgatgt agaaaaacaca tatttttaaa tggaaagaaaa ataaaaaggc 3597  
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 aaccactgc agaagctttt tttgagcact tggtggcattc agagcaggag gagcccccaga 3717  
 gccacactcg gtgtccccca ggctacactgc tcaggaaccc cttctgttct ctgagaactc 3777  
 aacagaggac attggctcac gcactgtgag attttgtttt tatacttgca actggtaat 3837  
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 ataataaaag aagtgcacaa gctgccgttgc acgttagctcg ag 3939

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 <213> Homo sapiens

<220>  
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 <222> (1)..(321)

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 1 5 10 15  
 cga gtg gca ctg ctg ctc ctg ctg gta gcc gct ggc cgg cgc gca 96  
 Arg Val Ala Leu Leu Leu Leu Leu Val Ala Ala Gly Arg Arg Ala  
 20 25 30

15/88

gca gga gcg tcc gtg gcc act gaa ctg cgc tgc cag tgc ttg cag acc	144		
Ala Gly Ala Ser Val Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr			
35	40	45	
ctg cag gga att cac ccc aag aac atc caa agt gtg aac gtg aag tcc	192		
Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys Ser			
50	55	60	
ccc gga ccc cac tgc gcc caa acc gaa gtc ata gcc aca ctc aag aat	240		
Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn			
65	70	75	80
ggg cg <sup>g</sup> aaa gct tgc ctc aat cct gca tcc ccc ata gtt aag aaa atc	288		
Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys Ile			
85	90	95	
atc gaa aag atg ctg aac agt gac aaa tcc aac tgaccagaag ggaggaggaa	341		
Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn			
100	105		
gctca <sup>c</sup> tgg <sup>t</sup> ggctgttcc <sup>t</sup> gaaggaggcc <sup>c</sup> ctgc <sup>c</sup> c <sup>t</sup> ttat <sup>t</sup> aggaacagaa <sup>g</sup> gaggaaagag <sup>g</sup> 401			
agacacagct <sup>t</sup> gcagaggcc <sup>a</sup> cctggattgt <sup>t</sup> gccta <sup>t</sup> atgt <sup>t</sup> tttgagc <sup>t</sup> atc <sup>t</sup> gcttaggaga <sup>t</sup> 461			
agtcttctat <sup>t</sup> ttat <sup>t</sup> tattt <sup>t</sup> attcattat <sup>t</sup> tttgaagatt <sup>t</sup> ctatgttaat <sup>t</sup> attttaggt <sup>t</sup> 521			
taaaataatt <sup>t</sup> aagggtat <sup>t</sup> ttaactctac <sup>t</sup> ctgcacactg <sup>t</sup> tcctattata <sup>t</sup> ttcattctt <sup>t</sup> 581			
ttgaaat <sup>t</sup> gtc <sup>t</sup> aaccccaagt <sup>t</sup> tagttcaatc <sup>t</sup> tggattcata <sup>t</sup> tttat <sup>t</sup> tg <sup>t</sup> a aggtagaat <sup>t</sup> g <sup>t</sup> 641			
ttttcaat <sup>t</sup> g <sup>t</sup> ttctccagtc <sup>t</sup> attatgttaa <sup>t</sup> tatttctgag <sup>t</sup> gagcctgcaa <sup>t</sup> catgccagcc <sup>t</sup> 701			
actgtgatag <sup>t</sup> aggctggcgg <sup>t</sup> atccaagcaa <sup>t</sup> atggccaaat <sup>t</sup> g <sup>t</sup> agatcattgt <sup>t</sup> gaaggcaggg <sup>t</sup> 761			
gaatgtat <sup>t</sup> gt <sup>t</sup> gcacatctgt <sup>t</sup> tttgtaactg <sup>t</sup> tttagatgaa <sup>t</sup> tg <sup>t</sup> cagttgt <sup>t</sup> tatttatt <sup>t</sup> ga <sup>t</sup> 821			
aatgatttca <sup>t</sup> cagtgtgtgg <sup>t</sup> tcaacatttc <sup>t</sup> tcatgtt <sup>t</sup> gaa <sup>t</sup> actttaagaa <sup>t</sup> ctaaaatgtt <sup>t</sup> 881			
ctaaatatcc <sup>t</sup> cttggacatt <sup>t</sup> ttatgtctt <sup>t</sup> cttgtaaggc <sup>t</sup> atactgc <sup>t</sup> ttt gtttaat <sup>t</sup> gg <sup>t</sup> 941			
agtttacag <sup>t</sup> tg <sup>t</sup> ttctggc <sup>t</sup> tt <sup>t</sup> agaacaaa <sup>t</sup> ggggcttaat <sup>t</sup> tattgat <sup>t</sup> gtt <sup>t</sup> tt <sup>t</sup> catagaga <sup>t</sup> 1001			
atataaaaat <sup>t</sup> aaagcactt <sup>t</sup> a <sup>t</sup> g <sup>t</sup> 1024			

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 <213> Homo sapiens

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 <220>  
 <221> modified\_base



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 agttttatg 1064

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 Met Arg Ile Ala Val  
 1 5

att tgc ttt tgc ctc cta ggc atc acc tgt gcc ata cca gtt aaa cag 164  
 Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala Ile Pro Val Lys Gln  
 10 15 20

gct gat tct gga agt tct gag gaa aag cag ctt tac aac aaa tac cca 212  
 Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu Tyr Asn Lys Tyr Pro  
 25 30 35

gat gct gtg gcc aca tgg cta aac cct gac cca tct cag aag cag aat 260  
 Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro Ser Gln Lys Gln Asn  
 40 45 50

ctc cta gcc cca cag acc ctt cca agt aag tcc aac gaa agc cat gac 308  
 Leu Leu Ala Pro Gln Thr Leu Pro Ser Lys Ser Asn Glu Ser His Asp  
 55 60 65

cac atg gat gat atg gat gat gaa gat gat gac cat gtg gac agc 356  
 His Met Asp Asp Met Asp Asp Glu Asp Asp Asp His Val Asp Ser  
 70 75 80 85

cag gac tcc att gac tcg aac gac tct gat gat gta gat gac act gat 404  
 Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp Val Asp Asp Thr Asp  
 90 95 100

gat tct cac cag tct gat gag tct cac cat tct gat gaa tct gat gaa 452  
 Asp Ser His Gln Ser Asp Glu Ser His His Ser Asp Glu Ser Asp Glu  
 105 110 115

ctg gtc act gat ttt ccc acg gac ctg cca gca acc gaa gtt ttc act 500  
 Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala Thr Glu Val Phe Thr  
 120 125 130

cca gtt gtc ccc aca gta gac aca tat gat ggc cga ggt gat agt gtg 548  
 Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly Arg Gly Asp Ser Val  
 135 140 145

gtt tat gga ctg agg tca aaa tct aag aag ttt cgc aga cct gac atc	596
Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe Arg Arg Pro Asp Ile	
150 155 160 165	
cag tac cct gat gct aca gac gag gac atc acc tca cac atg gaa agc	644
Gln Tyr Pro Asp Ala Thr Asp Glu Asp Ile Thr Ser His Met Glu Ser	
170 175 180	
gag gag ttg aat ggt gca tac aag gcc atc ccc gtt gcc cag gac ctg	692
Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro Val Ala Gln Asp Leu	
185 190 195	
aac gcg cct tct gat tgg gac agc cgt ggg aag gac agt tat gaa acg	740
Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser Tyr Glu Thr	
200 205 210	
agt cag ctg gat gac cag agt gct gaa acc cac agc cac aag cag tcc	788
Ser Gln Leu Asp Asp Gln Ser Ala Glu Thr His Ser His Lys Gln Ser	
215 220 225	
aga tta tat aag cgg aaa gcc aat gat gag agc aat gag cat tcc gat	836
Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser Asn Glu His Ser Asp	
230 235 240 245	
gtg att gat agt cag gaa ctt tcc aaa gtc agc cgt gaa ttc cac agc	884
Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser Arg Glu Phe His Ser	
250 255 260	
cat gaa ttt cac agc cat gaa gat atg ctg gtt gta gac ccc aaa agt	932
His Glu Phe His Ser His Glu Asp Met Leu Val Val Asp Pro Lys Ser	
265 270 275	
aag gaa gaa gat aaa cac ctg aaa ttt cgt att tct cat gaa tta gat	980
Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile Ser His Glu Leu Asp	
280 285 290	
agt gca tct tct gag gtc aat taaaaggaga aaaaatacaa tttctcaactt	1031
Ser Ala Ser Ser Glu Val Asn	
295 300	
tgcatttagt caaaaagaaaa aatgctttat agcaaatga aagagaacat gaaatgcttc	1091
tttctcagtt tattgggtga atgtgtatct atttgagtct ggaaataact aatgtgtttg	1151
ataattagtt tagttgtgg cttcatggaa actccctgta aactaaaagc ttcagggtta	1211
tgtctatgtt cattctatag aagaaatgca aactatcact gtatttaat atttgttatt	1271
ctctcatgaa tagaaattta tgtagaagca aacaaaatac ttttacccac taaaaaagag	1331
aatataacat tttatgtcac tataatctt tgaaaaaa gtttagtgtat attttgttgt	1391
gattatctt ttgtgggtgt aataaatctt ttatctgaa tgtaataaga aaaaaaaaaaa	1451
aaaaacaaaa aaaaaaaaaa	1469

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 <213> Homo sapiens

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 gcgcgggca gcagaagcga gagccgagcg cggacccagc caggacccac agccctcccc 120  
 agctgcccag gaagagcccc agcc atg gaa cac cag ctc ctg tgc tgc gaa 171  
 Met Glu His Gln Leu Leu Cys Cys Glu  
 1 5

gtg gaa acc atc cgc cgc gcg tac ccc gat gcc aac ctc ctc aac gac 219  
 Val Glu Thr Ile Arg Arg Ala Tyr Pro Asp Ala Asn Leu Leu Asn Asp  
 10 15 20 25

cgg gtg ctg cgg gcc atg ctg aag gcg gag gag acc tgc gcg ccc tcg 267  
 Arg Val Leu Arg Ala Met Leu Lys Ala Glu Glu Thr Cys Ala Pro Ser  
 30 35 40

gtg tcc tac ttc aaa tgt gtg cag aag gag gtc ctg ccc tcc atg cgg 315  
 Val Ser Tyr Phe Lys Cys Val Gln Lys Glu Val Leu Pro Ser Met Arg  
 45 50 55

aag atc gtc gcc acc tgg atg ctg gag gtc tgc gag gaa cag aag tgc 363  
 Lys Ile Val Ala Thr Trp Met Leu Glu Val Cys Glu Glu Gln Lys Cys  
 60 65 70

gag gag gag gtc ttc ccg ctg gcc atg aac tac ctg gac cgc ttc ctg 411  
 Glu Glu Val Phe Pro Leu Ala Met Asn Tyr Leu Asp Arg Phe Leu  
 75 80 85

tcg ctg gag ccc gtg aaa aag agc cgc ctg cag ctg ctg ggg gcc act 459  
 Ser Leu Glu Pro Val Lys Lys Ser Arg Leu Gln Leu Leu Gly Ala Thr  
 90 95 100 105

tgc atg ttc gtg gcc tct aag atg aag gag acc atc ccc ctg acg gcc 507  
 Cys Met Phe Val Ala Ser Lys Met Lys Glu Thr Ile Pro Leu Thr Ala  
 110 115 120

gag aag ctg tgc atc tac acc gac ggc tcc atc cgg ccc gag gag ctg 555  
 Glu Lys Leu Cys Ile Tyr Thr Asp Gly Ser Ile Arg Pro Glu Glu Leu  
 125 130 135

ctg caa atg gag ctg ctc ctg gtg aac aag ctc aag tgg aac ctg gcc 603  
 Leu Gln Met Glu Leu Leu Val Asn Lys Leu Lys Trp Asn Leu Ala  
 140 145 150

gca atg acc ccg cac gat ttc att gaa cac ttc ctc tcc aaa atg cca 651  
 Ala Met Thr Pro His Asp Phe Ile Glu His Phe Leu Ser Lys Met Pro  
 155 160 165

20/88

gag	gcf	gag	gag	aac	aaa	cag	atc	atc	cgf	aaa	cac	gcf	cag	acc	ttc	699	
Glu	Ala	Glu	Glu	Asn	Lys	Gln	Ile	Ile	Arg	Lys	His	Ala	Gln	Thr	Phe		
170							175								185		
gtt	gcc	tct	tgt	gcc	aca	gat	gtg	aag	ttc	att	tcc	aat	ccg	ccc	tcc	747	
Val	Ala	Ser	Cys	Ala	Thr	Asp	Val	Lys	Phe	Ile	Ser	Asn	Pro	Pro	Ser		
							190				195				200		
atg	gtg	gca	gcf	ggg	agc	gtg	gtg	gcc	gca	gtg	caa	gcf	ctg	aac	ctg	795	
Met	Val	Ala	Ala	Gly	Ser	Val	Val	Ala	Ala	Val	Gln	Gly	Leu	Asn	Leu		
							205				210				215		
agg	agc	ccc	aac	aac	ttc	ctg	tcc	tac	tac	cgf	ctc	aca	cgf	ttc	ctc	843	
Arg	Ser	Pro	Asn	Asn	Phe	Leu	Ser	Tyr	Tyr	Arg	Leu	Thr	Arg	Phe	Leu		
							220				225				230		
tcc	aga	gtg	atc	aag	tgt	gac	cca	gac	tgc	ctc	cgf	gcc	tgc	cag	gag	891	
Ser	Arg	Val	Ile	Lys	Cys	Asp	Pro	Asp	Cys	Leu	Arg	Ala	Cys	Gln	Glu		
							235				240				245		
cag	atc	gaa	gcc	ctg	ctg	gag	tca	agc	ctg	cgf	cag	gcc	cag	cag	aac	939	
Gln	Ile	Glu	Ala	Leu	Leu	Glu	Ser	Ser	Leu	Arg	Gln	Ala	Gln	Gln	Asn		
							250				255				260		
atg	gac	ccc	aag	gcc	gag	gag	gag	gag	gag	gag	gag	gag	gtg		987		
Met	Asp	Pro	Lys	Ala	Ala	Glu	Glu	Glu	Glu	Glu	Glu	Glu	Glu	Val			
							270				275				280		
gac	ctg	gct	tgc	aca	ccc	acc	gac	gtg	cgf	gac	gtg	gac	atc		1029		
Asp	Leu	Ala	Cys	Thr	Pro	Thr	Asp	Val	Arg	Asp	Val	Asp	Ile				
							285				290				295		
tgagggggccc	aggcaggcgg	gcgccaccgc	cacccgcagc	gagggcggag	ccggccccag	1089											
tgctccaca	tgacagtccc	tcctctccgg	agcattttga	taccagaagg	gaaagcttca	1149											
ttctccttgt	tgttggttgt	ttttccttt	gctttccc	cttccatct	ctgacttaag	1209											
caaaaagaaaa	agattacc	aaaactgtct	ttaaaagaga	gagagag		1256											

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 <222> (559) ..(1875)

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 ataaaaagccg gtttccgggg ctttatctaa ctcgctgttag taattccagc gagagggcaga 180

gggagcgagc gggcgccgg ctagggtgg aagccgggc gagcagagct gcgctgcggg 240  
 cgtcctggga agggagatcc ggagcgaata gggggcttcg cctctggccc agccctccc 300  
 cttgatcccc caggccagcg gtccgcaacc cttgccat ccacgaaact ttgcccata 360  
 cagcggcgag gcactttgca ctggaaactta caacacccga gcaaggacgc gactctccc 420  
 acgcggggag gctattctgc ccattgggg acactcccc gccgctgcca ggacccgctt 480  
 ctctgaaagg ctctccttgc agctgcttag acgctggatt ttttcgggt agtggaaaac 540  
 cagcagcctc ccgcgacg atg ccc ctc aac gtt agc ttc acc aac agg aac 591  
 Met Pro Leu Asn Val Ser Phe Thr Asn Arg Asn  
 1 5 10

tat gac ctc gac tac gac tcg gtg cag ccg tat ttc tac tgc gac gag 639  
 Tyr Asp Leu Asp Tyr Asp Ser Val Gln Pro Tyr Phe Tyr Cys Asp Glu  
 15 20 25

gag gag aac ttc tac cag cag cag cag agc gag ctg cag ccc ccg 687  
 Glu Glu Asn Phe Tyr Gln Gln Gln Gln Ser Glu Leu Gln Pro Pro  
 30 35 40

gcg ccc agc gag gat atc tgg aag aaa ttc gag ctg ctg ccc acc ccg 735  
 Ala Pro Ser Glu Asp Ile Trp Lys Lys Phe Glu Leu Leu Pro Thr Pro  
 45 50 55

ccc ctg tcc cct agc cgc cgc tcc ggg ctc tgc tgc ccc tcc tac gtt 783  
 Pro Leu Ser Pro Ser Arg Arg Ser Gly Leu Cys Ser Pro Ser Tyr Val  
 60 65 70 75

gcg gtc aca ccc ttc tcc ctt cgg gga gac aac gac ggc ggt ggc ggg 831  
 Ala Val Thr Pro Phe Ser Leu Arg Gly Asp Asn Asp Gly Gly Gly Gly  
 80 85 90

agc ttc tcc acg gcc gac cag ctg gag atg gtg acc gag ctg ctg gga 879  
 Ser Phe Ser Thr Ala Asp Gln Leu Glu Met Val Thr Glu Leu Leu Gly  
 95 100 105

gga gac atg gtg aac cag agt ttc atc tgc gac ccg gac gac gag acc 927  
 Gly Asp Met Val Asn Gln Ser Phe Ile Cys Asp Pro Asp Asp Glu Thr  
 110 115 120

ttc atc aaa aac atc atc atc cag gac tgt atg tgg agc ggc ttc tcg 975  
 Phe Ile Lys Asn Ile Ile Gln Asp Cys Met Trp Ser Gly Phe Ser  
 125 130 135

gcc gcc gcc aag ctc gtc tca gag aag ctg gcc tcc tac cag gct gcg 1023  
 Ala Ala Ala Lys Leu Val Ser Glu Lys Leu Ala Ser Tyr Gln Ala Ala  
 140 145 150 155

cgc aaa gac agc ggc agc ccg aac ccc gcc cgc ggc cac agc gtc tgc 1071  
 Arg Lys Asp Ser Gly Ser Pro Asn Pro Ala Arg Gly His Ser Val Cys  
 160 165 170

22/88

tcc acc tcc agc ttg tac ctg cag gat	ctg agc gcc gcc tca gag	1119	
Ser Thr Ser Ser Leu Tyr Leu Gln Asp	Leu Ser Ala Ala Ala Ser Glu		
175	180	185	
tgc atc gac ccc tcg gtg gtc ttc ccc tac cct ctc aac gac agc agc		1167	
Cys Ile Asp Pro Ser Val Val Phe Pro Tyr Pro	Leu Asn Asp Ser Ser		
190	195	200	
tcg ccc aag tcc tgc gcc tcg caa gac tcc agc gcc ttc tct ccg tcc		1215	
Ser Pro Lys Ser Cys Ala Ser Gln Asp Ser Ser	Ala Phe Ser Pro Ser		
205	210	215	
tcg gat tct ctg ctc tcc tcg acg gag tcc tcc ccg cag ggc agc ccc		1263	
Ser Asp Ser Leu Leu Ser Ser Thr Glu Ser Ser Pro Gln Gly Ser Pro			
220	225	230	235
gag ccc ctg gtg ctc cat gag gag aca ccg ccc acc acc agc agc gac		1311	
Glu Pro Leu Val Leu His Glu Glu Thr Pro Pro Thr Thr Ser Ser Asp			
240	245	250	
tct gag gag gaa caa gaa gat gag gaa gaa atc gat gtt gtt tct gtg		1359	
Ser Glu Glu Glu Gln Glu Asp Glu Glu Glu Ile Asp Val Val Ser Val			
255	260	265	
gaa aag agg cag gct cct ggc aaa agg tca gag tct gga tca cct tct		1407	
Glu Lys Arg Gln Ala Pro Gly Lys Arg Ser Glu Ser Gly Ser Pro Ser			
270	275	280	
gct gga ggc cac agc aaa cct cct cac agc cca ctg gtc ctc aag agg		1455	
Ala Gly Gly His Ser Lys Pro Pro His Ser Pro Leu Val Leu Lys Arg			
285	290	295	
tgc cac gtc tcc aca cat cag cac aac tac gca gcg cct ccc tcc act		1503	
Cys His Val Ser Thr His Gln His Asn Tyr Ala Ala Pro Pro Ser Thr			
300	305	310	315
cgg aag gac tat cct gct gcc aag agg gtc aag ttg gac agt gtc aga		1551	
Arg Lys Asp Tyr Pro Ala Ala Lys Arg Val Lys Leu Asp Ser Val Arg			
320	325	330	
gtc ctg aga cag atc agc aac aac cga aaa tgc acc agc ccc agg tcc		1599	
Val Leu Arg Gln Ile Ser Asn Asn Arg Lys Cys Thr Ser Pro Arg Ser			
335	340	345	
tcg gac acc gag gag aat gtc aag agg cga aca cac aac gtc ttg gag		1647	
Ser Asp Thr Glu Glu Asn Val Lys Arg Arg Thr His Asn Val Leu Glu			
350	355	360	
cgc cag agg agg aac gag cta aaa cgg agc ttt ttt gcc ctg cgt gac		1695	
Arg Gln Arg Arg Asn Glu Leu Lys Arg Ser Phe Phe Ala Leu Arg Asp			
365	370	375	
cag atc ccg gag ttg gaa aac aat gaa aag gcc ccc aag gta gtt atc		1743	
Gln Ile Pro Glu Leu Glu Asn Asn Glu Lys Ala Pro Lys Val Val Ile			
380	385	390	395

23/88

ctt aaa aaa gcc aca gca tac atc ctg tcc gtc caa gca gag gag caa	1791																								
Leu Lys Lys Ala Thr Ala Tyr Ile Leu Ser Val Gln Ala Glu Glu Gln																									
400	405		410	aag ctc att tct gaa gag gac ttg ttg cgaa aaa cga cga gaa cag ttg	1839	Lys Leu Ile Ser Glu Glu Asp Leu Leu Arg Lys Arg Arg Glu Gln Leu		415	420		425	aaa cac aaa ctt gaa cag cta cgg aac tct tgt gcg taaggaaaag	1885	Lys His Lys Leu Glu Gln Leu Arg Asn Ser Cys Ala		430	435	taagggaaaac gattccttct aacagaaaatg tcctgagcaa tcacctatga acttgtttca	1945	aatgcatgat caaatgcaac ctcacaacct tggctgagtc ttgagactga aagattttagc	2005	cataatgtaa actgcctcaa attggacttt gggcataaaaa gaacttttt atgcttacca	2065	tctttttttt ttctttaaca gatttgtatt taagaattgt ttttaaaaaa ttttaa	2121
	410																								
aag ctc att tct gaa gag gac ttg ttg cgaa aaa cga cga gaa cag ttg	1839																								
Lys Leu Ile Ser Glu Glu Asp Leu Leu Arg Lys Arg Arg Glu Gln Leu																									
415	420		425	aaa cac aaa ctt gaa cag cta cgg aac tct tgt gcg taaggaaaag	1885	Lys His Lys Leu Glu Gln Leu Arg Asn Ser Cys Ala		430	435	taagggaaaac gattccttct aacagaaaatg tcctgagcaa tcacctatga acttgtttca	1945	aatgcatgat caaatgcaac ctcacaacct tggctgagtc ttgagactga aagattttagc	2005	cataatgtaa actgcctcaa attggacttt gggcataaaaa gaacttttt atgcttacca	2065	tctttttttt ttctttaaca gatttgtatt taagaattgt ttttaaaaaa ttttaa	2121								
	425																								
aaa cac aaa ctt gaa cag cta cgg aac tct tgt gcg taaggaaaag	1885																								
Lys His Lys Leu Glu Gln Leu Arg Asn Ser Cys Ala																									
430	435																								
taagggaaaac gattccttct aacagaaaatg tcctgagcaa tcacctatga acttgtttca	1945																								
aatgcatgat caaatgcaac ctcacaacct tggctgagtc ttgagactga aagattttagc	2005																								
cataatgtaa actgcctcaa attggacttt gggcataaaaa gaacttttt atgcttacca	2065																								
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<222> (79)..(570)

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gcactcagag gaggcgcc atg tca gaa ccg gct ggg gat gtc cgt cag aac	111																																												
Met Ser Glu Pro Ala Gly Asp Val Arg Gln Asn																																													
1	5		10	cca tgc ggc agc aag gcc tgc cgc cgc ctc ttc ggc cca gtg gac agc	159	Pro Cys Gly Ser Lys Ala Cys Arg Leu Phe Gly Pro Val Asp Ser		15	20		25	gag cag ctg agc cgc gac tgt gat gcg cta atg gcg ggc tgc atc cag	207	Glu Gln Leu Ser Arg Asp Cys Asp Ala Leu Met Ala Gly Cys Ile Gln		30	35		40	gag gcc cgt gag cga tgg aac ttc gac ttt gtc acc gag aca cca ctg	255	Glu Ala Arg Glu Arg Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu		45	50		55	gag ggt gac ttc gcc tgg gag cgt gtg cggt ggc ctt ggc ctg ccc aag	303	Glu Gly Asp Phe Ala Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys		60	65		70		75	ctc tac ctt ccc acg ggg ccc cggt cga ggc cggt gat gag ttg gga gga	351	Leu Tyr Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly		80	85		90
	10																																												
cca tgc ggc agc aag gcc tgc cgc cgc ctc ttc ggc cca gtg gac agc	159																																												
Pro Cys Gly Ser Lys Ala Cys Arg Leu Phe Gly Pro Val Asp Ser																																													
15	20		25	gag cag ctg agc cgc gac tgt gat gcg cta atg gcg ggc tgc atc cag	207	Glu Gln Leu Ser Arg Asp Cys Asp Ala Leu Met Ala Gly Cys Ile Gln		30	35		40	gag gcc cgt gag cga tgg aac ttc gac ttt gtc acc gag aca cca ctg	255	Glu Ala Arg Glu Arg Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu		45	50		55	gag ggt gac ttc gcc tgg gag cgt gtg cggt ggc ctt ggc ctg ccc aag	303	Glu Gly Asp Phe Ala Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys		60	65		70		75	ctc tac ctt ccc acg ggg ccc cggt cga ggc cggt gat gag ttg gga gga	351	Leu Tyr Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly		80	85		90								
	25																																												
gag cag ctg agc cgc gac tgt gat gcg cta atg gcg ggc tgc atc cag	207																																												
Glu Gln Leu Ser Arg Asp Cys Asp Ala Leu Met Ala Gly Cys Ile Gln																																													
30	35		40	gag gcc cgt gag cga tgg aac ttc gac ttt gtc acc gag aca cca ctg	255	Glu Ala Arg Glu Arg Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu		45	50		55	gag ggt gac ttc gcc tgg gag cgt gtg cggt ggc ctt ggc ctg ccc aag	303	Glu Gly Asp Phe Ala Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys		60	65		70		75	ctc tac ctt ccc acg ggg ccc cggt cga ggc cggt gat gag ttg gga gga	351	Leu Tyr Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly		80	85		90																
	40																																												
gag gcc cgt gag cga tgg aac ttc gac ttt gtc acc gag aca cca ctg	255																																												
Glu Ala Arg Glu Arg Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu																																													
45	50		55	gag ggt gac ttc gcc tgg gag cgt gtg cggt ggc ctt ggc ctg ccc aag	303	Glu Gly Asp Phe Ala Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys		60	65		70		75	ctc tac ctt ccc acg ggg ccc cggt cga ggc cggt gat gag ttg gga gga	351	Leu Tyr Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly		80	85		90																								
	55																																												
gag ggt gac ttc gcc tgg gag cgt gtg cggt ggc ctt ggc ctg ccc aag	303																																												
Glu Gly Asp Phe Ala Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys																																													
60	65		70		75	ctc tac ctt ccc acg ggg ccc cggt cga ggc cggt gat gag ttg gga gga	351	Leu Tyr Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly		80	85		90																																
	70		75	ctc tac ctt ccc acg ggg ccc cggt cga ggc cggt gat gag ttg gga gga	351	Leu Tyr Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly		80	85		90																																		
	75																																												
ctc tac ctt ccc acg ggg ccc cggt cga ggc cggt gat gag ttg gga gga	351																																												
Leu Tyr Leu Pro Thr Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly																																													
80	85		90																																										
	90																																												

24/88

ggc agg cgg cct ggc acc tca cct gct ctg ctg cag ggg aca gca gag	399		
Gly Arg Arg Pro Gly Thr Ser Pro Ala Leu Leu Gln Gly Thr Ala Glu			
95	100	105	
gaa gac cat gtg gac ctg tca ctg tct tgt acc ctt gtg cct cgc tca	447		
Glu Asp His Val Asp Leu Ser Leu Ser Cys Thr Leu Val Pro Arg Ser			
110	115	120	
ggg gag cag gct gaa ggg tcc cca ggt gga cct gga gac tct cag ggt	495		
Gly Glu Gln Ala Glu Gly Ser Pro Gly Pro Gly Asp Ser Gln Gly			
125	130	135	
cga aaa cgg cgg cag acc agc atg aca gat ttc tac cac tcc aaa cgc	543		
Arg Lys Arg Arg Gln Thr Ser Met Thr Asp Phe Tyr His Ser Lys Arg			
140	145	150	155
cg <sup>g</sup> ctg atc ttc tcc aag agg aag ccc taatccgccc acaggaagcc	590		
Arg Leu Ile Phe Ser Lys Arg Lys Pro			
160			
tgca <sup>gt</sup> tc <sup>tc</sup> tg gaagcgc <sup>g</sup> ag ggc <sup>c</sup> tcaa <sup>a</sup> ag gccc <sup>c</sup> gtct <sup>a</sup> ta catcttct <sup>t</sup> gc cttagtct <sup>c</sup> ca 650			
gtttgtgtgt cttaattatt atttgtgttt taatttaa <sup>a</sup> ac acctcctcat gtacataaccc	710		
tggccgcccc ctgcccccca gcctctggca tt <sup>g</sup> agaattat tt <sup>aa</sup> acaaaaa actaggcgg <sup>t</sup>	770		
tgaatgagag gttcctaaga gtgctggca tt <sup>tt</sup> tatttt atgaaatact atttaaagcc	830		
tcctcatccc gtgttctc <sup>c</sup> t ttcctct <sup>t</sup> c cccggaggtt ggg <sup>t</sup> gggccc <sup>g</sup> g <sup>t</sup> ttcatgccc <sup>cc</sup> 890			
agctacttcc tc <sup>t</sup> tc <sup>cc</sup> ccac ttgtccgct <sup>g</sup> ggtggta <sup>c</sup> cc tctggagg <sup>gg</sup> t <sup>t</sup> gtggctc <sup>c</sup> t 950			
tccc <sup>c</sup> atcg <sup>c</sup> t gtcacagg <sup>g</sup> cg gttatgaa <sup>a</sup> at tcaccc <sup>c</sup> ctt tc <sup>t</sup> tg <sup>g</sup> acac tc <sup>g</sup> agac <sup>c</sup> tc <sup>g</sup> a 1010			
attcttttc atttgagaag taaacagat <sup>g</sup> g <sup>c</sup> a <sup>t</sup> t <sup>t</sup> gaa <sup>g</sup> ggggc <sup>c</sup> tc <sup>a</sup> c cgagtggggg 1070			
catcatcaaa aactttggag tccc <sup>c</sup> tcacc tc <sup>t</sup> c <sup>t</sup> taagg tt <sup>gg</sup> ggc <sup>gg</sup> tg <sup>g</sup> acc <sup>c</sup> ctgaa <sup>g</sup> 1130			
gtgagcacag cctagg <sup>g</sup> ctg agctgggac ctggta <sup>c</sup> cc cctggct <sup>t</sup> tt gatacccccc <sup>cc</sup> 1190			
tctgtctt <sup>t</sup> gt gaaggcaggg ggaagg <sup>t</sup> ggg gtcctggagc agaccacccc <sup>cc</sup> g <sup>c</sup> ctg <sup>cc</sup> c <sup>t</sup> c 1250			
atggccccc <sup>t</sup> c tgac <sup>c</sup> tc <sup>g</sup> cac tggggagccc <sup>cc</sup> g <sup>t</sup> tctc <sup>g</sup> agt <sup>t</sup> gt tgagc <sup>t</sup> ttt <sup>t</sup> gg <sup>g</sup> 1310			
ctccc <sup>c</sup> ctgta c <sup>t</sup> ttt <sup>t</sup> gagg agccccagct acc <sup>c</sup> tt <sup>t</sup> cttc tccagctgg <sup>gg</sup> ctctgcaatt <sup>t</sup> 1370			
ccc <sup>c</sup> ct <sup>t</sup> g <sup>c</sup> t g <sup>c</sup> tgtcc <sup>c</sup> c <sup>t</sup> ccc <sup>c</sup> ttgt <sup>c</sup> cc tttcc <sup>c</sup> ttca g <sup>t</sup> acc <sup>c</sup> ctc <sup>t</sup> agctccaggt <sup>gg</sup> 1430			
ggctctgagg tg <sup>c</sup> ctgtccc <sup>c</sup> cc acccccaccc <sup>c</sup> ccagct <sup>c</sup> aat ggact <sup>t</sup> ggaag <sup>g</sup> ggg <sup>a</sup> agg <sup>gg</sup> ac <sup>g</sup> 1490			
acacaagaag aagg <sup>gg</sup> cacccc tagttctacc <sup>t</sup> tc <sup>t</sup> aggcagct <sup>t</sup> caagcagcga <sup>g</sup> ccgcccccc <sup>t</sup> c <sup>t</sup> 1550			
ctctagctgt <sup>t</sup> gt ggggtgagg <sup>gg</sup> g <sup>t</sup> ccc <sup>c</sup> atgt <sup>t</sup> g <sup>g</sup> gtggcacagg <sup>gg</sup> ccccc <sup>t</sup> ttgag <sup>g</sup> tgggg <sup>t</sup> tat <sup>c</sup> 1610			
tctgtgttag <sup>t</sup> gg <sup>t</sup> tat <sup>t</sup> g <sup>a</sup> tg <sup>gg</sup> ggagta <sup>g</sup> gatctttct <sup>a</sup> ggagggagac <sup>g</sup> actggccc <sup>c</sup> t 1670			
caaatcg <sup>t</sup> cc <sup>c</sup> agcgac <sup>c</sup> ttc <sup>t</sup> c <sup>t</sup> catcc <sup>c</sup> acc <sup>c</sup> c <sup>c</sup> atcc <sup>c</sup> tcc <sup>c</sup> ccagttcatt <sup>t</sup> g <sup>c</sup> acttt <sup>t</sup> gat <sup>t</sup> 1730			

25/88

tagcagcgg acaaggagtc agacattta agatggtggc agtagaggct atggacaggg 1790  
 catgccacgt gggctcatat ggggctggga gtagttgtct ttccctggcac taacgtttag 1850  
 cccctggagg cactgaagtg ctttagtgtac ttggagtatt ggggtctgac cccaaacacc 1910  
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 gggtttcgt gttcacatc tcgtggttca cgggggagtg ggcagcgcca ggggcgcggc 180  
 cgcgtgtggc ctcgtgctg atgctactga ggagccagcg tctagggcag cagccgcttc 240  
 ctagaagacc aggtc atg atg atg ggc agc gcc cga gtg gcg gag ctg ctg 291  
 Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu  
 1 5 10  
 ctg ctc cac ggc gcg gag ccc aac tgc gcc gac ccc gcc act ctc acc 339  
 Leu Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu Thr  
 15 20 25  
 cga ccc gtg cac gac gct gcc cgg gag ggc ttc ctg gac acg ctg gtg 387  
 Arg Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val  
 30 35 40  
 gtg ctg cac cgg gcc ggg gcg cgg ctg gac gtg cgc gat gcc tgg ggc 435  
 Val Leu His Arg Ala Gly Ala Arg Leu Asp Val Arg Asp Ala Trp Gly  
 45 50 55 60  
 cgt ctg ccc gtg gac ctg gct gag gag ctg ggc cat cgc gat gtc gca 483  
 Arg Leu Pro Val Asp Leu Ala Glu Glu Leu Gly His Arg Asp Val Ala  
 65 70 75  
 cgg tac ctg cgc gcg gct gcg ggg ggc acc aga ggc agt aac cat gcc 531  
 Arg Tyr Leu Arg Ala Ala Gly Gly Thr Arg Gly Ser Asn His Ala  
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26/88

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ggcgcgctc agggaaaggcg ggtgcgcgccc tgccggggcg ag atg ggc agg ggg      174
                                         Met Gly Arg Gly
                                         1
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tca cct ctg gtg cca aag ggc ggc gca gcg gct gcc gag ctc ggc cct 270  
Ser Pro Leu Val Pro Lys Gly Gly Ala Ala Ala Ala Glu Leu Gly Pro  
25 30 35

gga ggc ggc gag aac atg gtg cgc agg ttc ttg gtg acc ctc cgg att 318  
Gly Gly Gly Glu Asn Met Val Arg Arg Phe Leu Val Thr Leu Arg Ile  
40 45 50

cgc cgc gcg tgc ggc ccg ccg cga gtg agg gtt ttc gtg gtt cac atc 366  
Arg Arg Ala Cys Gly Pro Pro Arg Val Arg Val Phe Val Val His Ile  
55 60 65

ccg cg<sup>70</sup> ctc acg ggg gag tgg gca g<sup>75</sup> cca ggg g<sup>80</sup> cg<sup>85</sup> ccc g<sup>90</sup> cc<sup>95</sup> gct gtg 414  
 Pro Arg Leu Thr Gly Glu Trp Ala Ala Pro Gly Ala Pro Ala Ala Val

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gcc ctc gtg ctg atg cta ctg agg agc cag cgt cta ggg cag cag ccg 462
Ala Leu Val Leu Met Leu Leu Arg Ser Gln Arg Leu Gly Gln Gln Pro
85          90          95          100
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27/88

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Leu Pro Arg Arg Pro Gly His Asp Asp Gly Gln Arg Pro Ser Gly Gly		
105	110	115
gct gct gct gct cca cgg cgc gga gcc caa ctg cgc cga ccc cgc cac	558	
Ala Ala Ala Ala Pro Arg Arg Gly Ala Gln Leu Arg Arg Pro Arg His		
120	125	130
tct cac ccg acc cgt gca cga cgc tgc ccg gga ggg ctt cct gga cac	606	
Ser His Pro Thr Arg Ala Arg Cys Pro Gly Gly Leu Pro Gly His		
135	140	145
gct ggt ggt gct gca ccg ggc cgg ggc gcg gct gga cgt gcg cga tgc	654	
Ala Gly Gly Ala Ala Pro Gly Arg Gly Ala Ala Gly Arg Ala Arg Cys		
150	155	160
ctg ggg ccg tct gcc cgt gga cct ggc tgaggagctg ggcgcgcgcgc	701	
Leu Gly Pro Ser Ala Arg Gly Pro Gly		
165	170	
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aacctcgaaa aacttagatc atcagtcacc gaaggtccta cagggccaca actgcggcc	881	
ccacaaccca ccccgcttc gtagtttca tttagaaaat agagcttttta aaaaatgtcct	941	
gccttttaac gtagatataat gcctttttt actaccgtaa atgtccattt atatcattt	1001	
ttatataattc ttataaaaat gtaaaaaaga aaaacaccgc ttctgcctt tcactgtgtt	1061	
ggagttttct ggagttagca ctcacgcct aagcgcacat tcatgtggc atttcttgcg	1121	
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 tgccagcaga ttcagtgtca tgtgaggacg tgcttcctgc ttcatagata agagcttgg 180

28/88

gctcggcgca caaccagcac catctggtcg cg atg gtg gac acg gaa agc cca	233
Met Val Asp Thr Glu Ser Pro	
1 5	
ctc tgc ccc ctc tcc cca ctc gag gcc ggc gat cta gag agc ccg tta	281
Leu Cys Pro Leu Ser Pro Leu Glu Ala Gly Asp Leu Glu Ser Pro Leu	
10 15 20	
tct gaa gag ttc ctg caa gaa atg gga aac atc caa gag att tcg caa	329
Ser Glu Glu Phe Leu Gln Glu Met Gly Asn Ile Gln Glu Ile Ser Gln	
25 30 35	
tcc atc ggc gag gat agt tct gga agc ttt ggc ttt acg gaa tac cag	377
Ser Ile Gly Glu Asp Ser Ser Gly Ser Phe Gly Phe Thr Glu Tyr Gln	
40 45 50 55	
tat tta gga agc tgt cct ggc tca gat ggc tcg gtc atc acg gac acg	425
Tyr Leu Gly Ser Cys Pro Gly Ser Asp Gly Ser Val Ile Thr Asp Thr	
60 65 70	
ctt tca cca gct tcg agc ccc tcc tcg gtg act tat cct gtg gtc ccc	473
Leu Ser Pro Ala Ser Ser Pro Ser Ser Val Thr Tyr Pro Val Val Pro	
75 80 85	
ggc agc gtg gac gag tct ccc agt gga gca ttg aac atc gaa tgt aga	521
Gly Ser Val Asp Glu Ser Pro Ser Gly Ala Leu Asn Ile Glu Cys Arg	
90 95 100	
atc tgc ggg gac aag gcc tca ggc tat cat tac gga gtc cac gcg tgt	569
Ile Cys Gly Asp Lys Ala Ser Gly Tyr His Tyr Gly Val His Ala Cys	
105 110 115	
gaa ggc tgc aag ggc ttc ttt cgg cga acg att cga ctc aag ctg gtg	617
Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr Ile Arg Leu Lys Leu Val	
120 125 130 135	
tat gac aag tgc gac cgc agc tgc aag atc cag aaa aag aac aga aac	665
Tyr Asp Lys Cys Asp Arg Ser Cys Lys Ile Gln Lys Lys Asn Arg Asn	
140 145 150	
aaa tgc cag tat tgt cga ttt cac aag tgc ctt tct gtc ggg atg tca	713
Lys Cys Gln Tyr Cys Arg Phe His Lys Cys Leu Ser Val Gly Met Ser	
155 160 165	
cac aac gcg att cgt ttt gga cga atg cca aga tct gag aaa gca aaa	761
His Asn Ala Ile Arg Phe Gly Arg Met Pro Arg Ser Glu Lys Ala Lys	
170 175 180	
ctg aaa gca gaa att ctt acc tgt gaa cat gac ata gaa gat tct gaa	809
Leu Lys Ala Glu Ile Leu Thr Cys Glu His Asp Ile Glu Asp Ser Glu	
185 190 195	
act gca gat ctc aaa tct ctg gcc aag aga atc tac gag gcc tac ttg	857
Thr Ala Asp Leu Lys Ser Leu Ala Lys Arg Ile Tyr Glu Ala Tyr Leu	
200 205 210 215	

29/88

aag aac ttc aac atg aac aag gtc aaa gcc cgg gtc atc ctc tca gga	905																																																																																																										
Lys Asn Phe Asn Met Asn Lys Val Lys Ala Arg Val Ile Leu Ser Gly																																																																																																											
220	225	230		aag gcc agt aac aat cca cct ttt gtc ata cat gat atg gag aca ctg	953	Lys Ala Ser Asn Asn Pro Pro Phe Val Ile His Asp Met Glu Thr Leu		235	240	245		tgt atg gct gag aag acg ctg gtg gcc aag ctg gtg gcc aat ggc atc	1001	Cys Met Ala Glu Lys Thr Leu Val Ala Lys Leu Val Ala Asn Gly Ile		250	255	260		cag aac aag gag gcg gag gtc cgc atc ttt cac tgc tgc cag tgc acg	1049	Gln Asn Lys Glu Ala Glu Val Arg Ile Phe His Cys Cys Gln Cys Thr		265	270	275		tca gtg gag acc gtc acg gag ctc acg gaa ttc gcc aag gcc atc cca	1097	Ser Val Glu Thr Val Thr Glu Leu Thr Glu Phe Ala Lys Ala Ile Pro		280	285	290	295	ggc ttc gca aac ttg gac ctg aac gat caa gtg aca ttg cta aaa tac	1145	Gly Phe Ala Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr		300	305	310		gga gtt tat gag gcc ata ttc gcc atg ctg tct tct gtg atg aac aaa	1193	Gly Val Tyr Glu Ala Ile Phe Ala Met Leu Ser Ser Val Met Asn Lys		315	320	325		gac ggg atg ctg gta gcg tat gga aat ggg ttt ata act cgt gaa ttc	1241	Asp Gly Met Leu Val Ala Tyr Gly Asn Gly Phe Ile Thr Arg Glu Phe		330	335	340		cta aaa agc cta agg aaa ccg ttc tgt gat atc atg gaa ccc aag ttt	1289	Leu Lys Ser Leu Arg Lys Pro Phe Cys Asp Ile Met Glu Pro Lys Phe		345	350	355		gat ttt gcc atg aag ttc aat gca ctg gaa ctg gat gac agt gat atc	1337	Asp Phe Ala Met Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Ile		360	365	370	375	tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt	1385	Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu		380	385	390		cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433	Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val		395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435	
230																																																																																																											
aag gcc agt aac aat cca cct ttt gtc ata cat gat atg gag aca ctg	953																																																																																																										
Lys Ala Ser Asn Asn Pro Pro Phe Val Ile His Asp Met Glu Thr Leu																																																																																																											
235	240	245		tgt atg gct gag aag acg ctg gtg gcc aag ctg gtg gcc aat ggc atc	1001	Cys Met Ala Glu Lys Thr Leu Val Ala Lys Leu Val Ala Asn Gly Ile		250	255	260		cag aac aag gag gcg gag gtc cgc atc ttt cac tgc tgc cag tgc acg	1049	Gln Asn Lys Glu Ala Glu Val Arg Ile Phe His Cys Cys Gln Cys Thr		265	270	275		tca gtg gag acc gtc acg gag ctc acg gaa ttc gcc aag gcc atc cca	1097	Ser Val Glu Thr Val Thr Glu Leu Thr Glu Phe Ala Lys Ala Ile Pro		280	285	290	295	ggc ttc gca aac ttg gac ctg aac gat caa gtg aca ttg cta aaa tac	1145	Gly Phe Ala Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr		300	305	310		gga gtt tat gag gcc ata ttc gcc atg ctg tct tct gtg atg aac aaa	1193	Gly Val Tyr Glu Ala Ile Phe Ala Met Leu Ser Ser Val Met Asn Lys		315	320	325		gac ggg atg ctg gta gcg tat gga aat ggg ttt ata act cgt gaa ttc	1241	Asp Gly Met Leu Val Ala Tyr Gly Asn Gly Phe Ile Thr Arg Glu Phe		330	335	340		cta aaa agc cta agg aaa ccg ttc tgt gat atc atg gaa ccc aag ttt	1289	Leu Lys Ser Leu Arg Lys Pro Phe Cys Asp Ile Met Glu Pro Lys Phe		345	350	355		gat ttt gcc atg aag ttc aat gca ctg gaa ctg gat gac agt gat atc	1337	Asp Phe Ala Met Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Ile		360	365	370	375	tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt	1385	Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu		380	385	390		cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433	Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val		395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435									
245																																																																																																											
tgt atg gct gag aag acg ctg gtg gcc aag ctg gtg gcc aat ggc atc	1001																																																																																																										
Cys Met Ala Glu Lys Thr Leu Val Ala Lys Leu Val Ala Asn Gly Ile																																																																																																											
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260																																																																																																											
cag aac aag gag gcg gag gtc cgc atc ttt cac tgc tgc cag tgc acg	1049																																																																																																										
Gln Asn Lys Glu Ala Glu Val Arg Ile Phe His Cys Cys Gln Cys Thr																																																																																																											
265	270	275		tca gtg gag acc gtc acg gag ctc acg gaa ttc gcc aag gcc atc cca	1097	Ser Val Glu Thr Val Thr Glu Leu Thr Glu Phe Ala Lys Ala Ile Pro		280	285	290	295	ggc ttc gca aac ttg gac ctg aac gat caa gtg aca ttg cta aaa tac	1145	Gly Phe Ala Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr		300	305	310		gga gtt tat gag gcc ata ttc gcc atg ctg tct tct gtg atg aac aaa	1193	Gly Val Tyr Glu Ala Ile Phe Ala Met Leu Ser Ser Val Met Asn Lys		315	320	325		gac ggg atg ctg gta gcg tat gga aat ggg ttt ata act cgt gaa ttc	1241	Asp Gly Met Leu Val Ala Tyr Gly Asn Gly Phe Ile Thr Arg Glu Phe		330	335	340		cta aaa agc cta agg aaa ccg ttc tgt gat atc atg gaa ccc aag ttt	1289	Leu Lys Ser Leu Arg Lys Pro Phe Cys Asp Ile Met Glu Pro Lys Phe		345	350	355		gat ttt gcc atg aag ttc aat gca ctg gaa ctg gat gac agt gat atc	1337	Asp Phe Ala Met Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Ile		360	365	370	375	tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt	1385	Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu		380	385	390		cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433	Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val		395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435																									
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tca gtg gag acc gtc acg gag ctc acg gaa ttc gcc aag gcc atc cca	1097																																																																																																										
Ser Val Glu Thr Val Thr Glu Leu Thr Glu Phe Ala Lys Ala Ile Pro																																																																																																											
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290	295																																																																																																										
ggc ttc gca aac ttg gac ctg aac gat caa gtg aca ttg cta aaa tac	1145																																																																																																										
Gly Phe Ala Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr																																																																																																											
300	305	310		gga gtt tat gag gcc ata ttc gcc atg ctg tct tct gtg atg aac aaa	1193	Gly Val Tyr Glu Ala Ile Phe Ala Met Leu Ser Ser Val Met Asn Lys		315	320	325		gac ggg atg ctg gta gcg tat gga aat ggg ttt ata act cgt gaa ttc	1241	Asp Gly Met Leu Val Ala Tyr Gly Asn Gly Phe Ile Thr Arg Glu Phe		330	335	340		cta aaa agc cta agg aaa ccg ttc tgt gat atc atg gaa ccc aag ttt	1289	Leu Lys Ser Leu Arg Lys Pro Phe Cys Asp Ile Met Glu Pro Lys Phe		345	350	355		gat ttt gcc atg aag ttc aat gca ctg gaa ctg gat gac agt gat atc	1337	Asp Phe Ala Met Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Ile		360	365	370	375	tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt	1385	Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu		380	385	390		cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433	Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val		395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435																																									
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gga gtt tat gag gcc ata ttc gcc atg ctg tct tct gtg atg aac aaa	1193																																																																																																										
Gly Val Tyr Glu Ala Ile Phe Ala Met Leu Ser Ser Val Met Asn Lys																																																																																																											
315	320	325		gac ggg atg ctg gta gcg tat gga aat ggg ttt ata act cgt gaa ttc	1241	Asp Gly Met Leu Val Ala Tyr Gly Asn Gly Phe Ile Thr Arg Glu Phe		330	335	340		cta aaa agc cta agg aaa ccg ttc tgt gat atc atg gaa ccc aag ttt	1289	Leu Lys Ser Leu Arg Lys Pro Phe Cys Asp Ile Met Glu Pro Lys Phe		345	350	355		gat ttt gcc atg aag ttc aat gca ctg gaa ctg gat gac agt gat atc	1337	Asp Phe Ala Met Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Ile		360	365	370	375	tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt	1385	Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu		380	385	390		cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433	Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val		395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435																																																	
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gac ggg atg ctg gta gcg tat gga aat ggg ttt ata act cgt gaa ttc	1241																																																																																																										
Asp Gly Met Leu Val Ala Tyr Gly Asn Gly Phe Ile Thr Arg Glu Phe																																																																																																											
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340																																																																																																											
cta aaa agc cta agg aaa ccg ttc tgt gat atc atg gaa ccc aag ttt	1289																																																																																																										
Leu Lys Ser Leu Arg Lys Pro Phe Cys Asp Ile Met Glu Pro Lys Phe																																																																																																											
345	350	355		gat ttt gcc atg aag ttc aat gca ctg gaa ctg gat gac agt gat atc	1337	Asp Phe Ala Met Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Ile		360	365	370	375	tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt	1385	Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu		380	385	390		cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433	Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val		395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435																																																																	
355																																																																																																											
gat ttt gcc atg aag ttc aat gca ctg gaa ctg gat gac agt gat atc	1337																																																																																																										
Asp Phe Ala Met Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Ile																																																																																																											
360	365	370	375	tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt	1385	Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu		380	385	390		cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433	Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val		395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435																																																																									
370	375																																																																																																										
tcc ctt ttt gtg gct gct atc att tgc tgt gga gat cgt cct ggc ctt	1385																																																																																																										
Ser Leu Phe Val Ala Ala Ile Ile Cys Cys Gly Asp Arg Pro Gly Leu																																																																																																											
380	385	390		cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433	Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val		395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435																																																																																	
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cta aac gta gga cac att gaa aaa atg cag gag ggt att gta cat gtg	1433																																																																																																										
Leu Asn Val Gly His Ile Glu Lys Met Gln Glu Gly Ile Val His Val																																																																																																											
395	400	405		ctc aga ctc cac ctg cag agc aac cac ccg gac gat atc ttt ctc ttc	1481	Leu Arg Leu His Leu Gln Ser Asn His Pro Asp Asp Ile Phe Leu Phe		410	415	420		cca aaa ctt ctt caa aaa atg gca gac ctc cgg cag ctg gtg acg gag	1529	Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu		425	430	435																																																																																									
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30/88

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 Met Gly Glu Thr Leu Gly Asp  
 1 5  
  
 tct cct att gac cca gaa agc gat tcc ttc act gat aca ctg tct gca 160  
 Ser Pro Ile Asp Pro Glu Ser Asp Ser Phe Thr Asp Thr Leu Ser Ala  
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 Asn Ile Ser Gln Glu Met Thr Met Val Asp Thr Glu Met Pro Phe Trp  
 25 30 35  
  
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 Pro Thr Asn Phe Gly Ile Ser Ser Val Asp Leu Ser Val Met Glu Asp  
 40 45 50 55  
  
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 His Ser His Ser Phe Asp Ile Lys Pro Phe Thr Thr Val Asp Phe Ser  
 60 65 70  
  
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 Ser Ile Ser Thr Pro His Tyr Glu Asp Ile Pro Phe Thr Arg Thr Asp  
 75 80 85  
  
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 Pro Val Val Ala Asp Tyr Lys Tyr Asp Leu Lys Leu Gln Glu Tyr Gln  
 90 95 100

31/88

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act cag ctc tac aat aag cct cat gaa gag cct tcc aac tcc ctc atg	496
Thr Gln Leu Tyr Asn Lys Pro His Glu Glu Pro Ser Asn Ser Leu Met	
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gca att gaa tgt cgt gtc tgt gga gat aaa gct tct gga ttt cac tat	544
Ala Ile Glu Cys Arg Val Cys Gly Asp Lys Ala Ser Gly Phe His Tyr	
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Gly Val His Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr Ile	
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Arg Leu Lys Leu Ile Tyr Asp Arg Cys Asp Leu Asn Cys Arg Ile His	
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Lys Lys Ser Arg Asn Lys Cys Gln Tyr Cys Arg Phe Gln Lys Cys Leu	
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gcc gag aag gag aag ctg ttg gcg gag atc tcc agt gat atc gac cag	784
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Leu Asn Pro Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu Tyr	
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Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala	
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atc ttg aca gga aag aca aca gac aaa tca cca ttc gtt atc tat gac	928
Ile Leu Thr Gly Lys Thr Asp Lys Ser Pro Phe Val Ile Tyr Asp	
265 270 275	
atg aat tcc tta atg atg gga gaa gat aaa atc aag ttc aaa cac atc	976
Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His Ile	
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acc ccc ctg cag gag cag agc aaa gag gtg gcc atc cgc atc ttt cag	1024
Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe Gln	
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ggc tgc cag ttt cgc tcc gtg gag gct gtg cag gag atc aca gag tat	1072
Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu Tyr	
315 320 325	

32/88

gcc aaa agc att cct ggt ttt gta aat ctt gac ttg aac gac caa gta	1120
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act ctc ctc aaa tat gga gtc cac gag atc att tac aca atg ctg gcc	1168
Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu Ala	
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Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly Phe	
360 365 370 375	
atg aca agg gag ttt cta aag agc ctg cga aag cct ttt ggt gac ttt	1264
Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp Phe	
380 385 390	
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Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu Leu	
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Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile Leu Ser Gly	
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Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln Asp	
425 430 435	
aac ctg cta caa gcc ctg gag ctc cag ctg aag ctg aac cac cct gag	1456
Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro Glu	
440 445 450 455	
tcc tca cag ctg ttt gcc aag ctg ctc cag aaa atg aca gac ctc aga	1504
Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg	
460 465 470	
cag att gtc acg gaa cac gtg cag cta ctg cag gtg atc aag aag acg	1552
Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys Thr	
475 480 485	
gag aca gac atg agt ctt cac ccg ctc ctg cag gag atc tac aag gac	1600
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Met Glu Gln Pro Gln Glu
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Glu Ala Pro Glu Val Arg Glu Glu Glu Lys Glu Glu Val Ala Glu
10 15 20

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Ala Glu Gly Ala Pro Glu Leu Asn Gly Gly Pro Gln His Ala Leu Pro
25 30 35

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Ser Ser Ser Tyr Thr Asp Leu Ser Arg Ser Ser Pro Pro Ser Leu
40 45 50

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Leu Asp Gln Leu Gln Met Gly Cys Asp Gly Ala Ser Cys Gly Ser Leu
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75 80 85

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Gly Val His Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr Ile
90 95 100

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105 110 115

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Lys Lys Asn Arg Asn Lys Cys Gln Tyr Cys Arg Phe Gln Lys Cys Leu
120 125 130

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135 140 145 150

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34/88

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tac aat gcc tac ctg aaa aac ttc aac atg acc aaa aag aag gcc cgc Tyr Asn Ala Tyr Leu Lys Asn Phe Asn Met Thr Lys Lys Ala Arg 185 190 195	931
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gtt acc ctt ctc aag tat ggc gtg cac gag gcc atc ttc gcc atg ctg Val Thr Leu Leu Lys Tyr Gly Val His Glu Ala Ile Phe Ala Met Leu 280 285 290	1219
gcc tct atc gtc aac aag gac ggg ctg ctg gta gcc aac ggc agt ggc Ala Ser Ile Val Asn Lys Asp Gly Leu Leu Val Ala Asn Gly Ser Gly 295 300 305 310	1267
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ctt gat gac agt gac ctg gcc cta ttc att gcg gcc atc att ctg tgt Leu Asp Asp Ser Asp Leu Ala Leu Phe Ile Ala Ala Ile Ile Leu Cys 345 350 355	1411
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35/88

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Thr Glu Thr Glu Thr Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys	
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Asp Met Tyr	
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36/88

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 ccagctcctt tcgcccgcgc cctccgttcg ctccggacac c atg gac aag ttt tgg 176  
 Met Asp Lys Phe Trp  
 1 5  
  
 tgg cac gca gcc tgg gga ctc tgc ctc gtg ccg ctg agc ctg gcg cag 224  
 Trp His Ala Ala Trp Gly Leu Cys Leu Val Pro Leu Ser Leu Ala Gln  
 10 15 20  
  
 atc gat ttg aat ata acc tgc cgc ttt gca ggt gta ttc cac gtg gag 272  
 Ile Asp Leu Asn Ile Thr Cys Arg Phe Ala Gly Val Phe His Val Glu  
 25 30 35  
  
 aaa aat ggt cgc tac agc atc tct cgg acg gag gcc gct gac ctc tgc 320  
 Lys Asn Gly Arg Tyr Ser Ile Ser Arg Thr Glu Ala Ala Asp Leu Cys  
 40 45 50  
  
 aag gct ttc aat agc acc ttg ccc aca atg gcc cag atg gag aaa gct 368  
 Lys Ala Phe Asn Ser Thr Leu Pro Thr Met Ala Gln Met Glu Lys Ala  
 55 60 65  
  
 ctg agc atc gga ttt gag acc tgc agg tat ggg ttc ata gaa ggg cac 416  
 Leu Ser Ile Gly Phe Glu Thr Cys Arg Tyr Gly Phe Ile Glu Gly His  
 70 75 80 85

37/88

gtg gtg att ccc cg <sup>g</sup> atc cac ccc aac tcc atc t <sup>g</sup> t gca gca aac aac	90	95	100	464
Val Val Ile Pro Arg Ile His Pro Asn Ser Ile Cys Ala Ala Asn Asn				
aca ggg gtg tac atc ctc aca tcc aac acc tcc cag tat gac aca tat	105	110	115	512
Thr Gly Val Tyr Ile Leu Thr Ser Asn Thr Ser Gln Tyr Asp Thr Tyr				
tgc ttc aat gct tca gct cca cct gaa gaa gat t <sup>g</sup> t aca tca gtc aca	120	125	130	560
Cys Phe Asn Ala Ser Ala Pro Pro Glu Glu Asp Cys Thr Ser Val Thr				
gac ctg ccc aat gcc ttt gat gga cca att acc ata act att gtt aac	135	140	145	608
Asp Leu Pro Asn Ala Phe Asp Gly Pro Ile Thr Ile Thr Ile Val Asn				
cgt gat ggc acc cgc tat gtc cag aaa gga gaa tac aga acg aat cct	150	155	160	656
Arg Asp Gly Thr Arg Tyr Val Gln Lys Gly Glu Tyr Arg Thr Asn Pro				
gaa gac atc tac ccc agc aac cct act gat gat gac gtg agc agc ggc	170	175	180	704
Glu Asp Ile Tyr Pro Ser Asn Pro Thr Asp Asp Asp Val Ser Ser Gly				
tcc tcc agt gaa agg agc agc act tca gga ggt tac atc ttt tac acc	185	190	195	752
Ser Ser Ser Glu Arg Ser Ser Thr Ser Gly Gly Tyr Ile Phe Tyr Thr				
ttt tct act gta cac ccc atc cca gac gaa gac agt ccc tgg atc acc	200	205	210	800
Phe Ser Thr Val His Pro Ile Pro Asp Glu Asp Ser Pro Trp Ile Thr				
gac agc aca gac aga atc cct gct acc act ttg atg agc act agt gct	215	220	225	848
Asp Ser Thr Asp Arg Ile Pro Ala Thr Thr Leu Met Ser Thr Ser Ala				
aca gca act gag aca gca acc aag agg caa gaa acc tgg gat tgg ttt	230	235	240	896
Thr Ala Thr Glu Thr Ala Thr Lys Arg Gln Glu Thr Trp Asp Trp Phe				
tca tgg ttg ttt cta cca tca gag tca aag aat cat ctt cac aca aca	250	255	260	944
Ser Trp Leu Phe Leu Pro Ser Glu Ser Lys Asn His Leu His Thr Thr				
aca caa atg gct ggt acg tct tca aat acc atc tca gca ggc tgg gag	265	270	275	992
Thr Gln Met Ala Gly Thr Ser Ser Asn Thr Ile Ser Ala Gly Trp Glu				
cca aat gaa gaa aat gaa gat gaa aga gac aga cac ctc agt ttt tct	280	285	290	1040
Pro Asn Glu Glu Asn Glu Asp Glu Arg Asp Arg His Leu Ser Phe Ser				
gga tca ggc att gat gat gat gaa gat ttt atc tcc agc acc att tca	295	300	305	1088
Gly Ser Gly Ile Asp Asp Asp Glu Asp Phe Ile Ser Ser Thr Ile Ser				

38/88

acc aca cca cg	gct ttt gac cac aca aaa cag aac cag gac tgg acc	1136	
Thr Thr Pro Arg Ala Phe Asp His Thr Lys Gln Asn Gln Asp Trp Thr			
310	315	320	325
cag tgg aac cca agc cat tca aat ccg gaa gtg cta ctt cag aca acc	1184		
Gln Trp Asn Pro Ser His Ser Asn Pro Glu Val Leu Leu Gln Thr Thr			
330	335	340	
aca agg atg act gat gta gac aga aat ggc acc act gct tat gaa gga	1232		
Thr Arg Met Thr Asp Val Asp Arg Asn Gly Thr Thr Ala Tyr Glu Gly			
345	350	355	
aac tgg aac cca gaa gca cac cct ccc ctc att cac cat gag cat cat	1280		
Asn Trp Asn Pro Glu Ala His Pro Pro Leu Ile His His Glu His His			
360	365	370	
gag gaa gaa gag acc cca cat tct aca agc aca atc cag gca act cct	1328		
Glu Glu Glu Glu Thr Pro His Ser Thr Ser Thr Ile Gln Ala Thr Pro			
375	380	385	
agt agt aca acg gaa gaa aca gct acc cag aag gaa cag tgg ttt ggc	1376		
Ser Ser Thr Thr Glu Glu Thr Ala Thr Gln Lys Glu Gln Trp Phe Gly			
390	395	400	405
aac aga tgg cat gag gga tat cgc caa aca ccc aaa gaa gac tcc cat	1424		
Asn Arg Trp His Glu Gly Tyr Arg Gln Thr Pro Lys Glu Asp Ser His			
410	415	420	
tcg aca aca ggg aca gct gca gcc tca gct cat acc agc cat cca atg	1472		
Ser Thr Thr Gly Thr Ala Ala Ser Ala His Thr Ser His Pro Met			
425	430	435	
caa gga agg aca aca cca agc cca gag gac agt tcc tgg act gat ttc	1520		
Gln Gly Arg Thr Thr Pro Ser Pro Glu Asp Ser Ser Trp Thr Asp Phe			
440	445	450	
ttc aac cca atc tca cac ccc atg gga cga ggt cat caa gca gga aga	1568		
Phe Asn Pro Ile Ser His Pro Met Gly Arg Gly His Gln Ala Gly Arg			
455	460	465	
agg atg gat atg gac tcc agt cat agt ata acg ctt cag cct act gca	1616		
Arg Met Asp Met Asp Ser Ser His Ser Ile Thr Leu Gln Pro Thr Ala			
470	475	480	485
aat cca aac aca ggt ttg gtg gaa gat ttg gac agg aca gga cct ctt	1664		
Asn Pro Asn Thr Gly Leu Val Glu Asp Leu Asp Arg Thr Gly Pro Leu			
490	495	500	
tca atg aca acg cag cag agt aat tct cag agc ttc tct aca tca cat	1712		
Ser Met Thr Thr Gln Gln Ser Asn Ser Gln Ser Phe Ser Thr Ser His			
505	510	515	
gaa ggc ttg gaa gaa gat aaa gac cat cca aca act tct act ctg aca	1760		
Glu Gly Leu Glu Glu Asp Lys Asp His Pro Thr Thr Ser Thr Leu Thr			
520	525	530	

tca agc aat agg aat gat gtc aca ggt gga aga aga gac cca aat cat	1808
Ser Ser Asn Arg Asn Asp Val Thr Gly Gly Arg Arg Asp Pro Asn His	
535 540 545	
tct gaa ggc tca act act tta ctg gaa ggt tat acc tct cat tac cca	1856
Ser Glu Gly Ser Thr Thr Leu Leu Glu Gly Tyr Thr Ser His Tyr Pro	
550 555 560 565	
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His Thr Lys Glu Ser Arg Thr Phe Ile Pro Val Thr Ser Ala Lys Thr	
570 575 580	
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Gly Ser Phe Gly Val Thr Ala Val Thr Val Gly Asp Ser Asn Ser Asn	
585 590 595	
gtc aat cgt tcc tta tca gga gac caa gac aca ttc cac ccc agt ggg	2000
Val Asn Arg Ser Leu Ser Gly Asp Gln Asp Thr Phe His Pro Ser Gly	
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Gly Ser His Thr Thr His Gly Ser Glu Ser Asp Gly His Ser His Gly	
615 620 625	
agt caa gaa ggt gga gca aac aca acc tct ggt cct ata agg aca ccc	2096
Ser Gln Glu Gly Gly Ala Asn Thr Thr Ser Gly Pro Ile Arg Thr Pro	
630 635 640 645	
caa att cca gaa tgg ctg atc atc ttg gca tcc ctc ttg gcc ttg gct	2144
Gln Ile Pro Glu Trp Leu Ile Ile Leu Ala Ser Leu Leu Ala Leu Ala	
650 655 660	
ttg att ctt gca gtt tgc att gca gtc aac agt cga aga agg tgt ggg	2192
Leu Ile Leu Ala Val Cys Ile Ala Val Asn Ser Arg Arg Arg Cys Gly	
665 670 675	
cag aag aaa aag cta gtg atc aac agt ggc aat gga gct gtg gag gac	2240
Gln Lys Lys Leu Val Ile Asn Ser Gly Asn Gly Ala Val Glu Asp	
680 685 690	
aga aag cca agt gga ctc aac gga gag gcc agc aag tct cag gaa atg	2288
Arg Lys Pro Ser Gly Leu Asn Gly Glu Ala Ser Lys Ser Gln Glu Met	
695 700 705	
gtg cat ttg gtg aac aag gag tcg tca gaa act cca gac cag ttt atg	2336
Val His Leu Val Asn Lys Glu Ser Ser Gly Glu Thr Pro Asp Gln Phe Met	
710 715 720 725	
aca gct gat gag aca agg aac ctg cag aat gtg gac atg aag att ggg	2384
Thr Ala Asp Glu Thr Arg Asn Leu Gln Asn Val Asp Met Lys Ile Gly	
730 735 740	
gtg taacacctac accattatct tggaaagaaa caaccgttgg aaacataacc	2437
Val	
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 ccctggatca gtccttgc cagtataatt tttaaagtt actttgtcag aggcacaaaaa 3037  
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 agggcatctg tgtccgccttc ggccttgacc gctaccagtg tgactgcacc cgcacgggct 180  
 attccggccc caactgcacc atccctggcc tggacctg gctccggaaat tcaactgcggc 240  
 ccagccccctc tttcacccac ttccctgctca ctcacgggcg ctgggtctgg gagttgtca 300  
 atgccacctt catccgagag atg ctc atg cgc ctg gta ctc aca gtg cgc tcc 353  
 Met Leu Met Arg Leu Val Leu Thr Val Arg Ser  
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aac ctt atc ccc agt ccc ccc acc tac aac tca gca cat gac tac atc 401  
 Asn Leu Ile Pro Ser Pro Pro Thr Tyr Asn Ser Ala His Asp Tyr Ile  
 15 20 25

agc tgg gag tct ttc tcc aac gtg agc tat tac act cgt att ctg ccc 449  
 Ser Trp Glu Ser Phe Ser Asn Val Ser Tyr Tyr Arg Ile Leu Pro  
 30 35 40

tct gtg cct aaa gat tgc ccc aca ccc atg gga acc aaa ggg aag aag 497  
 Ser Val Pro Lys Asp Cys Pro Thr Pro Met Gly Thr Lys Gly Lys Lys  
 45 50 55

41/88

cag ttg cca gat gcc cag ctc ctg gcc cgc cgc ttc ctg ctc agg agg	545
Gln Leu Pro Asp Ala Gln Leu Leu Ala Arg Arg Phe Leu Leu Arg Arg	
60 65 70 75	
aag ttc ata cct gac ccc caa ggc acc aac ctc atg ttt gcc ttc ttt	593
Lys Phe Ile Pro Asp Pro Gln Gly Thr Asn Leu Met Phe Ala Phe Phe	
80 85 90	
gca caa cac ttc acc cac cag ttc ttc aaa act tct ggc aag atg ggt	641
Ala Gln His Phe Thr His Gln Phe Phe Lys Thr Ser Gly Lys Met Gly	
95 100 105	
cct ggc ttc acc aag gcc ttg ggc cat ggg gta gac ctc ggc cac att	689
Pro Gly Phe Thr Lys Ala Leu Gly His Gly Val Asp Leu Gly His Ile	
110 115 120	
tat gga gac aat ctg gag cgt cag tat caa ctg cgg ctc ttt aag gat	737
Tyr Gly Asp Asn Leu Glu Arg Gln Tyr Gln Leu Arg Leu Phe Lys Asp	
125 130 135	
ggg aaa ctc aag tac cag gtg ctg gat gga gaa atg tac ccg ccc tcg	785
Gly Lys Leu Lys Tyr Gln Val Leu Asp Gly Glu Met Tyr Pro Pro Ser	
140 145 150 155	
gta gaa gag gcg cct gtg ttg atg cac tac ccc cga ggc atc ccg ccc	833
Val Glu Glu Ala Pro Val Leu Met His Tyr Pro Arg Gly Ile Pro Pro	
160 165 170	
cag aqc cag atg gct gtg ggc cag gag gtg ttt ggg ctg ctt cct ggg	881
Gln Ser Gln Met Ala Val Gly Gln Glu Val Phe Gly Leu Leu Pro Gly	
175 180 185	
ctc atg ctg tat gcc acg ctc tgg cta cgt gag cac aac cgt gtg tgt	929
Leu Met Leu Tyr Ala Thr Leu Trp Leu Arg Glu His Asn Arg Val Cys	
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Asp Leu Leu Lys Ala Glu His Pro Thr Trp Gly Asp Glu Gln Leu Phe	
205 210 215	
cag acg acc cgc ctc atc ctc ata ggg gag acc atc aag att gtc atc	1025
Gln Thr Thr Arg Leu Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile	
220 225 230 235	
gag gag tac gtg cag cag ctg agt ggc tat ttc ctg cag ctg aaa ttt	1073
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240 245 250	
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Asp Pro Glu Leu Leu Phe Gly Val Gln Phe Gln Tyr Arg Asn Arg Ile	
255 260 265	
gcc atg gag ttc aac cat ctc tac cac tgg cac ccc ctc atg cct gac	1169
Ala Met Glu Phe Asn His Leu Tyr His Trp His Pro Leu Met Pro Asp	
270 275 280	

42/88

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Ser Phe Lys Val Gly Ser Gln Glu Tyr Ser Tyr Glu Gln Phe Leu Phe	
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aac acc tcc atg ttg gtg gac tat ggg gtt gag gcc ctg gtg gat gcc	1265
Asn Thr Ser Met Leu Val Asp Tyr Gly Val Glu Ala Leu Val Asp Ala	
300 305 310 315	
ttc tct cgc cag att gct ggc cgg atc ggt ggg ggc agg aac atg gac	1313
Phe Ser Arg Gln Ile Ala Gly Arg Ile Gly Gly Arg Asn Met Asp	
320 325 330	
cac cac atc ctg cat gtg gct gtg gat gtc atc agg gag tct cgg gag	1361
His His Ile Leu His Val Ala Val Asp Val Ile Arg Glu Ser Arg Glu	
335 340 345	
atg cgg ctg cag ccc ttc aat gag tac cgc aag agg ttt ggc atg aaa	1409
Met Arg Leu Gln Pro Phe Asn Glu Tyr Arg Lys Arg Phe Gly Met Lys	
350 355 360	
ccc tac acc tcc ttc cag gag ctc gta gga gag aag gag atg gca gca	1457
Pro Tyr Thr Ser Phe Gln Glu Leu Val Gly Glu Lys Glu Met Ala Ala	
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Glu Leu Glu Leu Tyr Gly Asp Ile Asp Ala Leu Glu Phe Tyr Pro	
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Gly Leu Leu Leu Glu Lys Cys His Pro Asn Ser Ile Phe Gly Glu Ser	
400 405 410	
atg ata gag att ggg gct ccc ttt tcc ctc aag ggt ctc cta ggg aat	1601
Met Ile Glu Ile Gly Ala Pro Phe Ser Leu Lys Gly Leu Leu Gly Asn	
415 420 425	
ccc atc tgt tct ccg gag tac tgg aag ccg agc aca ttt ggc ggc gag	1649
Pro Ile Cys Ser Pro Glu Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu	
430 435 440	
gtg ggc ttt aac att gtc aag acg gcc aca ctg aag aag ctg gtc tgc	1697
Val Gly Phe Asn Ile Val Lys Thr Ala Thr Leu Lys Lys Leu Val Cys	
445 450 455	
ctc aac acc aag acc tgt ccc tac gtt tcc ttc cgt gtg ccg gat gcc	1745
Leu Asn Thr Lys Thr Cys Pro Tyr Val Ser Phe Arg Val Pro Asp Ala	
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Ser Gln Asp Asp Gly Pro Ala Val Glu Arg Pro Ser Thr Glu	
480 485	
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tgctgaggcc agggctgatg gtcttaatg ctcattttct ggttggcat ggtgagtgtt	1907
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43/88

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 Asp Gly Thr Glu Lys Arg Gly Arg Gly Arg Pro Arg Lys Gln Pro Pro  
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aag gag ccc agc gaa gtg cca aca cct aag aga cct cgg ggc cga cca 381  
 Lys Glu Pro Ser Glu Val Pro Thr Pro Lys Arg Pro Arg Gly Arg Pro  
 35 40 45 50

aag gga agc aaa aac aag ggt gct gcc aag acc cgg aaa acc acc aca 429  
 Lys Gly Ser Lys Asn Lys Gly Ala Ala Lys Thr Arg Lys Thr Thr Thr  
 55 60 65

44/88

act cca gga agg aaa cca agg ggc aga ccc aaa aaa ctg gag aag gag 477  
Thr Pro Gly Arg Lys Pro Arg Gly Arg Pro Lys Lys Leu Glu Lys Glu  
70 75 80

gaa gag gag ggc atc tcg cag gag tcc tcg gag gag gag cag 519  
Glu Glu Glu Gly Ile Ser Gln Glu Ser Ser Glu Glu Glu Gln  
85 90 95

tgaccatgc gtgccgcctg ctcctcaactg gaggagcagc ttcctctgg gactggacag 579  
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agccatttcc ccctcctcag atggggcacc aataacaagg agctcaccct gcccgcctcc 1419  
aaccggccctc ctgctcctcc ctgccccca aggttctggg tccattttc ctctgttccac 1479  
aaactacctc tggacagttg tttttttt tttcaatgt tccattttc gacatccggtc 1539  
attgctgctg ctaccagcgc caaatgttca tcctcattgc ctccctttct gcccacgatc 1599  
ccctccccca agataactctt tgtggggaaag agggggctggg gcatggcagg ctgggtgacc 1659  
gactacccca gtcccaggga aggtgcctg cccctaggat gctgcagcag agtgagcaag 1719  
ggggccccaa tcgaccataa aggggtgttagg ggccacctcc tccccctgtt ctgttgggg 1779  
ggggtagcca tgatttgtcc cagcctgggg ctccctctct ggtttccat ttacagttac 1839  
ttgaataaaa aaaatatcct tttctggaaa aaaaaaa 1875

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<210> 21
<211> 626
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (96) .. (332)

<400> 21
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cgctctcggt tcattttctg cagcgcgcca cgagg atg gcc cac aag cag atc 113
Met Ala His Lys Gln Ile
1 5

tac tac tcg gac aag tac ttc gac gaa cac tac gag tac cgg cat gtt 161
Tyr Tyr Ser Asp Lys Tyr Phe Asp Glu His Tyr Glu Tyr Arg His Val
10 15 20

atg tta ccc aga gaa ctt tcc aaa caa gta cct aaa act cat ctg atg 209
Met Leu Pro Arg Glu Leu Ser Lys Gln Val Pro Lys Thr His Leu Met
25 30 35

tct gaa gag gag tgg agg aga ctt ggt gtc caa cag agt cta ggc tgg 257
Ser Glu Glu Glu Trp Arg Arg Leu Gly Val Gln Gln Ser Leu Gly Trp
40 45 50

gtt cat tac atg att cat gag cca gaa cca cat att ctt ctc ttt aga 305
Val His Tyr Met Ile His Glu Pro Glu Pro His Ile Leu Leu Phe Arg
55 60 65 70

cga cct ctt cca aaa gat caa caa aaa tgaagtttat ctggggatcg 352
Arg Pro Leu Pro Lys Asp Gln Gln Lys
75

tcaaatctt ttcaaattt aatgtatgt gtatataagg tagtattcag tgaatacttg 412
agaaatgtac aatctttca tccatacctg tgcatgagct gtattcttca cagcaacaga 472
gctcagttaa atgcaactgc aagtaggtta ctgtaagatg tttaagataa aagttcttcc 532
agtcaagttt tctcttaagt gcctgttga gtttactgaa acagttact tttgttcaat 592
aaagttgt a tttgcattt aaaaaaaaaa aaaa 626

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<210> 22
<211> 3480
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (268) .. (2922)

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 tccgtcccgat ccaccgtccg cagctggtag ccagcctgcc cctcgccctcg actcccttcc 120  
 accaacacccg acacccacat tgacacccatcc agtccggcca gccgctccac tcgttgcctt 180  
 tgcatctcca cacatggcgt cctcgcccgag agcggccggct cctccggggg acccgccggtc 240  
 cccaccgtgc agcggggcat catcaag atg gtc ctc tca ggg tgc gcc atc att 294  
 Met Val Leu Ser Gly Cys Ala Ile Ile  
 1 5

gtc cga ggt cag cct cgt ggt ggg cct cct gag cgg cag atc aac 342  
 Val Arg Gly Gln Pro Arg Gly Gly Pro Pro Pro Glu Arg Gln Ile Asn  
 10 15 20 25

ctc agc aac att cgt gct gga aat ctt gct cgc cgg gca gcc gcc aca 390  
 Leu Ser Asn Ile Arg Ala Gly Asn Leu Ala Arg Arg Ala Ala Thr  
 30 35 40

caa cct gat gca aag gat acc cct gat gag ccc tgg gca ttt cca gct 438  
 Gln Pro Asp Ala Lys Asp Thr Pro Asp Glu Pro Trp Ala Phe Pro Ala  
 45 50 55

cga gag ttc ctt cga aag aag ctg att ggg aag gaa gtc tgt ttc acg 486  
 Arg Glu Phe Leu Arg Lys Lys Leu Ile Gly Lys Glu Val Cys Phe Thr  
 60 65 70

ata gaa aac aag act ccc cag ggg cga gag tat ggc atg atc tac ctt 534  
 Ile Glu Asn Lys Thr Pro Gln Gly Arg Glu Tyr Gly Met Ile Tyr Leu  
 75 80 85

gga aaa gat acc aat ggg gaa aac att gca gaa tca ctg gtt gca gag 582  
 Gly Lys Asp Thr Asn Gly Glu Asn Ile Ala Glu Ser Leu Val Ala Glu  
 90 95 100 105

ggc tta gcc acc cgg aga gaa ggc atg aga gct aat aat cct gag cag 630  
 Gly Leu Ala Thr Arg Arg Glu Gly Met Arg Ala Asn Asn Pro Glu Gln  
 110 115 120

aac cgg ctt tca gaa tgt gaa gaa caa gca aag gca gcc aag aaa ggg 678  
 Asn Arg Leu Ser Glu Cys Glu Glu Gln Ala Lys Ala Ala Lys Lys Gly  
 125 130 135

atg tgg agt gag ggg aac ggt tca cat act atc cgg gat ctc aag tat 726  
 Met Trp Ser Glu Gly Asn Gly Ser His Thr Ile Arg Asp Leu Lys Tyr  
 140 145 150

acc att gaa aac cca agg cac ttt gtg gac tca cac cac cag aag cct 774  
 Thr Ile Glu Asn Pro Arg His Phe Val Asp Ser His His Gln Lys Pro  
 155 160 165

gtt aat gct atc atc gag cat gtg cgg gac ggc agt gtg gtc agg gcc 822  
 Val Asn Ala Ile Ile Glu His Val Arg Asp Gly Ser Val Val Arg Ala  
 170 175 180 185

47/88

ctg ctc ctc cca gat tac tac ctg gtt aca gtc atg ctg tca ggc atc Leu Leu Leu Pro Asp Tyr Tyr Leu Val Thr Val Met Leu Ser Gly Ile 190 195 200	870
aag tgc cca act ttt cga cgg gaa gca gat ggc agt gaa act cca gag Lys Cys Pro Thr Phe Arg Arg Glu Ala Asp Gly Ser Glu Thr Pro Glu 205 210 215	918
cct ttt gct gca gaa gcc aaa ttt ttc act gag tcg cga ctg ctt cag Pro Phe Ala Ala Glu Ala Lys Phe Phe Thr Glu Ser Arg Leu Leu Gln 220 225 230	966
aga gat gtt cag atc att ctg gag agc tgc cac aac cag aac att gtg Arg Asp Val Gln Ile Ile Leu Glu Ser Cys His Asn Gln Asn Ile Val 235 240 245	1014
ggt acc atc ctt cat cca aat ggc aac atc aca gag ctc ctc ctg aag Gly Thr Ile Leu His Pro Asn Gly Asn Ile Thr Glu Leu Leu Leu Lys 250 255 260 265	1062
gaa ggt ttc gca cgc tgt gtg gac tgg tcg att gca gtt tac acc cgg Glu Gly Phe Ala Arg Cys Val Asp Trp Ser Ile Ala Val Tyr Thr Arg 270 275 280	1110
ggc gca gaa aag ctg agg gcg gca gag agg ttt gcc aaa gag cgc agg Gly Ala Glu Lys Leu Arg Ala Ala Glu Arg Phe Ala Lys Glu Arg Arg 285 290 295	1158
ctg aga ata tgg aga gac tat gtg gct ccc aca gct aat ttg gac caa Leu Arg Ile Trp Arg Asp Tyr Val Ala Pro Thr Ala Asn Leu Asp Gln 300 305 310	1206
aag gac aag cag ttt gtt gcc aag gtg atg cag gtt ctg aat gct gat Lys Asp Lys Gln Phe Val Ala Lys Val Met Gln Val Leu Asn Ala Asp 315 320 325	1254
gcc att gtt gtg aag ctg aac tca ggc gat tac aag acg att cac ctg Ala Ile Val Val Lys Leu Asn Ser Gly Asp Tyr Lys Thr Ile His Leu 330 335 340 345	1302
tcc agc atc cga cca ccg agg ctg gag ggg gag aac acc cag gat aag Ser Ser Ile Arg Pro Pro Arg Leu Glu Gly Glu Asn Thr Gln Asp Lys 350 355 360	1350
aac aag aaa ctg cgt ccc ctg tat gac att cct tac atg ttt gag gcc Asn Lys Lys Leu Arg Pro Leu Tyr Asp Ile Pro Tyr Met Phe Glu Ala 365 370 375	1398
cgg gaa ttt ctt cga aaa aag ctt att ggg aag aag gtc aat gtg acg Arg Glu Phe Leu Arg Lys Lys Leu Ile Gly Lys Lys Val Asn Val Thr 380 385 390	1446
gtg gac tac att aga cca gcc agc cca gcc aca gag aca gtg cct gcc Val Asp Tyr Ile Arg Pro Ala Ser Pro Ala Thr Glu Thr Val Pro Ala 395 400 405	1494

48/88

ttt tca gag cgt acc tgt gcc act gtc acc att gga gga ata aac att	1542
Phe Ser Glu Arg Thr Cys Ala Thr Val Thr Ile Gly Gly Ile Asn Ile	
410 415 420 425	
gct gag gct ctt gtc agc aaa ggt cta gcc aca gtg atc aga tac cg	1590
Ala Glu Ala Leu Val Ser Lys Gly Leu Ala Thr Val Ile Arg Tyr Arg	
430 435 440	
cag gat gat gac cag aga tca tca cac tac gat gaa ctg ctt gct gca	1638
Gln Asp Asp Asp Gln Arg Ser Ser His Tyr Asp Glu Leu Leu Ala Ala	
445 450 455	
gag gcc aga gct att aag aat ggc aaa gga ttg cat agc aag aag gaa	1686
Glu Ala Arg Ala Ile Lys Asn Gly Lys Gly Leu His Ser Lys Lys Glu	
460 465 470	
gtg cct atc cac cgt gtt gca gat ata tct ggg gat acc caa aaa gca	1734
Val Pro Ile His Arg Val Ala Asp Ile Ser Gly Asp Thr Gln Lys Ala	
475 480 485	
aag cag ttc ctg cct ttt ctt cag cgg gca ggt cgt tct gaa gct gtg	1782
Lys Gln Phe Leu Pro Phe Leu Gln Arg Ala Gly Arg Ser Glu Ala Val	
490 495 500 505	
gtg gaa tac gtc ttc agt ggt tct cgt ctc aaa ctc tat ttg cca aag	1830
Val Glu Tyr Val Phe Ser Gly Ser Arg Leu Lys Leu Tyr Leu Pro Lys	
510 515 520	
gaa act tgc ctt atc acc ttc ttg ctt gca ggc att gaa tgc ccc aga	1878
Glu Thr Cys Leu Ile Thr Phe Leu Leu Ala Gly Ile Glu Cys Pro Arg	
525 530 535	
gga gcc cga aac ctc cca ggc ttg gtg cag gaa gga gag ccc ttc agc	1926
Gly Ala Arg Asn Leu Pro Gly Leu Val Gln Glu Gly Glu Pro Phe Ser	
540 545 550	
gag gaa gct aca ctt ttc acc aag gaa ctg gtg ctg cag cga gag gtg	1974
Glu Glu Ala Thr Leu Phe Thr Lys Glu Leu Val Leu Gln Arg Glu Val	
555 560 565	
gag gtg gag gtg gag agc atg gac aag gcc ggc aac ttt atc ggc tgg	2022
Glu Val Glu Val Glu Ser Met Asp Lys Ala Gly Asn Phe Ile Gly Trp	
570 575 580 585	
ctg cac atc gac ggt gcc aac ctg tcc gtc ctg ctg gtg gag cac gcg	2070
Leu His Ile Asp Gly Ala Asn Leu Ser Val Leu Leu Val Glu His Ala	
590 595 600	
ctc tcc aag gtc cac ttc acc gcc gaa cgc agc tcc tac tac aag tcc	2118
Leu Ser Lys Val His Phe Thr Ala Glu Arg Ser Ser Tyr Tyr Lys Ser	
605 610 615	
ctg ctg tct gcc gag gag gcc gca aag cag aag aaa gag aag gtc tgg	2166
Leu Leu Ser Ala Glu Glu Ala Ala Lys Gln Lys Lys Glu Lys Val Trp	
620 625 630	

49/88

gcc cac tat gag gag cag ccc gtg gag gag gtg atg cca gtg ctg gag	2214
Ala His Tyr Glu Glu Gln Pro Val Glu Val Met Pro Val Leu Glu	
635 640 645	
gag aag gag cga tct gct agc tac aag ccc gtg ttt gtg acc gag atc	2262
Glu Lys Glu Arg Ser Ala Ser Tyr Lys Pro Val Phe Val Thr Glu Ile	
650 655 660 665	
act gat gac ctg cac ttc tac gtg cag gat gtg gag acc ggc acc cag	2310
Thr Asp Asp Leu His Phe Tyr Val Gln Asp Val Glu Thr Gly Thr Gln	
670 675 680	
ttc cag aag ctg atg gag aac atg cgc aat gac att gcc agt cac ccc	2358
Phe Gln Lys Leu Met Glu Asn Met Arg Asn Asp Ile Ala Ser His Pro	
685 690 695	
cct gta gag ggc tcc tat gcc ccc cgc agg gga gag ttc tgc att gcc	2406
Pro Val Glu Gly Ser Tyr Ala Pro Arg Arg Gly Glu Phe Cys Ile Ala	
700 705 710	
aaa ttt gta gat gga gaa tgg tac cgt gcc cga gta gag aaa gtc gag	2454
Lys Phe Val Asp Gly Glu Trp Tyr Arg Ala Arg Val Glu Lys Val Glu	
715 720 725	
tct cct gcc aaa ata cat gtc ttc tac att gac tac ggc aac aga gag	2502
Ser Pro Ala Lys Ile His Val Phe Tyr Ile Asp Tyr Gly Asn Arg Glu	
730 735 740 745	
gtc ctg cca tcc acc cgc ctg ggt acc cta tca cct gcc ttc agc aat	2550
Val Leu Pro Ser Thr Arg Leu Gly Thr Leu Ser Pro Ala Phe Ser Thr	
750 755 760	
cgg gtg ctg cca gct caa gcc acg gag tat gcc ttc gcc ttc atc cag	2598
Arg Val Leu Pro Ala Gln Ala Thr Glu Tyr Ala Phe Ala Phe Ile Gln	
765 770 775	
gtg ccc caa gat gat gat gcc cgc acg gac gcc gtg gac agc gta gtt	2646
Val Pro Gln Asp Asp Ala Arg Thr Asp Ala Val Asp Ser Val Val	
780 785 790	
cgg gat atc cag aac act cag tgc ctg ctc aac gtg gaa cac ctg agt	2694
Arg Asp Ile Gln Asn Thr Gln Cys Leu Leu Asn Val Glu His Leu Ser	
795 800 805	
gcc ggc tgc ccc cat gtc acc ctg cag ttt gca gat tcc aag ggc gat	2742
Ala Gly Cys Pro His Val Thr Leu Gln Phe Ala Asp Ser Lys Gly Asp	
810 815 820 825	
gtg ggg ctg ggc ttg gtg aag gaa ggg ctg gtc atg gtg gag gtg cgc	2790
Val Gly Leu Gly Leu Val Lys Glu Gly Leu Val Met Val Glu Val Arg	
830 835 840	
aag gag aaa cag ttc cag aaa gtg atc aca gaa tac ctg aat gcc caa	2838
Lys Glu Lys Gln Phe Gln Lys Val Ile Thr Glu Tyr Leu Asn Ala Gln	
845 850 855	

50/88

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gag tca gcc aag agc gcc agg ctg aac ctg tgg cgc tat gga gac ttt 2886
Glu Ser Ala Lys Ser Ala Arg Leu Asn Leu Trp Arg Tyr Gly Asp Phe
860 865 870

cga gct gat gat gca gac gaa ttt ggc tac agc cgc taaggagggg 2932
Arg Ala Asp Asp Ala Asp Glu Phe Gly Tyr Ser Arg
875 880 . 885

atcgggtttg gcccccagcc cccgtcacgc cagtcctct tcctctgccg ggaggggttt 2992
ttcaactcca aaccccagag aggggttgtt cattgggtcc agctttgttt cagtgtgtgg 3052
aaatgtctcg tgggtggca tcggggctgc ggggtgggaa ccccaaggtt ttctggggca 3112
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tctgatacgt ccattctcaa atgccagttt gttcacatct tcgctctggc cagcccattc 3412
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caaaaaaaaaa 3480

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<210> 23  
<211> 67  
<212> PRT  
<213> *Homo sapiens*

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<400> 23
Met Thr Ser Lys Leu Ala Val Ala Leu Leu Ala Ala Phe Leu Ile Ser
      1           5           10           15

Ala Ala Leu Cys Glu Gly Ala Val Leu Pro Arg Ser Ala Lys Glu Leu
      20          25          30

Arg Cys Gln Cys Ile Lys Thr Tyr Ser Lys Pro Phe His Pro Lys Phe
      35          40          45

Ile Lys Glu Leu Arg Val Ile Glu Ser Gly Pro His Cys Ala Asn Thr
      50          55          60

Glu Ile Met
      65

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<210> 24  
<211> 604  
<212> PRT  
<213> *Homo sapiens*

51/88

<400> 24  
Met Leu Ala Arg Ala Leu Leu Leu Cys Ala Val Leu Ala Leu Ser His  
1 5 10 15  
  
Thr Ala Asn Pro Cys Cys Ser His Pro Cys Gln Asn Arg Gly Val Cys  
20 25 30  
  
Met Ser Val Gly Phe Asp Gln Tyr Lys Cys Asp Cys Thr Arg Thr Gly  
35 40 45  
  
Phe Tyr Gly Glu Asn Cys Ser Thr Pro Glu Phe Leu Thr Arg Ile Lys  
50 55 60  
  
Leu Phe Leu Lys Pro Thr Pro Asn Thr Val His Tyr Ile Leu Thr His  
65 70 75 80  
  
Phe Lys Gly Phe Trp Asn Val Val Asn Asn Ile Pro Phe Leu Arg Asn  
85 90 95  
  
Ala Ile Met Ser Tyr Val Leu Thr Ser Arg Ser His Leu Ile Asp Ser  
100 105 110  
  
Pro Pro Thr Tyr Asn Ala Asp Tyr Gly Tyr Lys Ser Trp Glu Ala Phe  
115 120 125  
  
Ser Asn Leu Ser Tyr Tyr Arg Ala Leu Pro Pro Val Pro Asp Asp  
130 135 140  
  
Cys Pro Thr Pro Leu Gly Val Lys Gly Lys Lys Gln Leu Pro Asp Ser  
145 150 155 160  
  
Asn Glu Ile Val Glu Lys Leu Leu Arg Arg Lys Phe Ile Pro Asp  
165 170 175  
  
Pro Gln Gly Ser Asn Met Met Phe Ala Phe Phe Ala Gln His Phe Thr  
180 185 190  
  
His Gln Phe Phe Lys Thr Asp His Lys Arg Gly Pro Ala Phe Thr Asn  
195 200 205  
  
Gly Leu Gly His Gly Val Asp Leu Asn His Ile Tyr Gly Glu Thr Leu  
210 215 220  
  
Ala Arg Gln Arg Lys Leu Arg Leu Phe Lys Asp Gly Lys Met Lys Tyr  
225 230 235 240  
  
Gln Ile Ile Asp Gly Glu Met Tyr Pro Pro Thr Val Lys Asp Thr Gln  
245 250 255  
  
Ala Glu Met Ile Tyr Pro Pro Gln Val Pro Glu His Leu Arg Phe Ala  
260 265 270  
  
Val Gly Gln Glu Val Phe Gly Leu Val Pro Gly Leu Met Met Tyr Ala  
275 280 285  
  
Thr Ile Trp Leu Arg Glu His Asn Arg Val Cys Asp Val Leu Lys Gln  
290 295 300

52/88

Glu His Pro Glu Trp Gly Asp Glu Gln Leu Phe Gln Thr Ser Arg Leu  
305 310 315 320

Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile Glu Asp Tyr Val Gln  
325 330 335

His Leu Ser Gly Tyr His Phe Lys Leu Lys Phe Asp Pro Glu Leu Leu  
340 345 350

Phe Asn Lys Gln Phe Gln Tyr Gln Asn Arg Ile Ala Ala Glu Phe Asn  
355 360 365

Thr Leu Tyr His Trp His Pro Leu Leu Pro Asp Thr Phe Gln Ile His  
370 375 380

Asp Gln Lys Tyr Asn Tyr Gln Gln Phe Ile Tyr Asn Asn Ser Ile Leu  
385 390 395 400

Leu Glu His Gly Ile Thr Gln Phe Val Glu Ser Phe Thr Arg Gln Ile  
405 410 415

Ala Gly Arg Val Ala Gly Gly Arg Asn Val Pro Pro Ala Val Gln Lys  
420 425 430

Val Ser Gln Ala Ser Ile Asp Gln Ser Arg Gln Met Lys Tyr Gln Ser  
435 440 445

Phe Asn Glu Tyr Arg Lys Arg Phe Met Leu Lys Pro Tyr Glu Ser Phe  
450 455 460

Glu Glu Leu Thr Gly Glu Lys Glu Met Ser Ala Glu Leu Glu Ala Leu  
465 470 475 480

Tyr Gly Asp Ile Asp Ala Val Glu Leu Tyr Pro Ala Leu Leu Val Glu  
485 490 495

Lys Pro Arg Pro Asp Ala Ile Phe Gly Glu Thr Met Val Glu Val Gly  
500 505 510

Ala Pro Phe Ser Leu Lys Gly Leu Met Gly Asn Val Ile Cys Ser Pro  
515 520 525

Ala Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Gln Ile  
530 535 540

Ile Asn Thr Ala Ser Ile Gln Ser Leu Ile Cys Asn Asn Val Lys Gly  
545 550 555 560

Cys Pro Phe Thr Ser Phe Ser Val Pro Asp Pro Glu Leu Ile Lys Thr  
565 570 575

Val Thr Ile Asn Ala Ser Ser Arg Ser Gly Leu Asp Asp Ile Asn  
580 585 590

Pro Thr Val Leu Leu Lys Glu Arg Ser Thr Glu Leu  
595 600

<210> 25  
<211> 360  
<212> PRT  
<213> Homo sapiens

<400> 25  
Met Glu Asp Phe Asn Met Glu Ser Asp Ser Phe Glu Asp Phe Trp Lys  
1 5 10 15

Gly Glu Asp Leu Ser Asn Tyr Ser Tyr Ser Ser Thr Leu Pro Pro Phe  
20 25 30

Leu Leu Asp Ala Ala Pro Cys Glu Pro Glu Ser Leu Glu Ile Asn Lys  
35 40 45

Tyr Phe Val Val Ile Ile Tyr Ala Leu Val Phe Leu Leu Ser Leu Leu  
50 55 60

Gly Asn Ser Leu Val Met Leu Val Ile Leu Tyr Ser Arg Val Gly Arg  
65 70 75 80

Ser Val Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ala Asp Leu Leu  
85 90 95

Phe Ala Leu Thr Leu Pro Ile Trp Ala Ala Ser Lys Val Asn Gly Trp  
100 105 110

Ile Phe Gly Thr Phe Leu Cys Lys Val Val Ser Leu Leu Lys Glu Val  
115 120 125

Asn Phe Tyr Ser Gly Ile Leu Leu Leu Ala Cys Ile Ser Val Asp Arg  
130 135 140

Tyr Leu Ala Ile Val His Ala Thr Arg Thr Leu Thr Gln Lys Arg Tyr  
145 150 155 160

Leu Val Lys Phe Ile Cys Leu Ser Ile Trp Gly Leu Ser Leu Leu  
165 170 175

Ala Leu Pro Val Leu Leu Phe Arg Arg Thr Val Tyr Ser Ser Asn Val  
180 185 190

Ser Pro Ala Cys Tyr Glu Asp Met Gly Asn Asn Thr Ala Asn Trp Arg  
195 200 205

Met Leu Leu Arg Ile Leu Pro Gln Ser Phe Gly Phe Ile Val Pro Leu  
210 215 220

Leu Ile Met Leu Phe Cys Tyr Gly Phe Thr Leu Arg Thr Leu Phe Lys  
225 230 235 240

Ala His Met Gly Gln Lys His Arg Ala Met Arg Val Ile Phe Ala Val  
245 250 255

Val Leu Ile Phe Leu Leu Cys Trp Leu Pro Tyr Asn Leu Val Leu  
260 265 270

54/88

Ala Asp Thr Leu Met Arg Thr Gln Val Ile Gln Glu Thr Cys Glu Arg  
 275 280 285

Arg Asn His Ile Asp Arg Ala Leu Asp Ala Thr Glu Ile Leu Gly Ile  
 290 295 300

Leu His Ser Cys Leu Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys  
 305 310 315 320

Phe Arg His Gly Leu Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser  
 325 330 335

Lys Asp Ser Leu Pro Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser  
 340 345 350

Ser Gly His Thr Ser Thr Thr Leu  
 355 360

<210> 26  
 <211> 198  
 <212> PRT  
 <213> Homo sapiens

<400> 26  
 Met Pro Leu Gly Leu Leu Trp Leu Gly Leu Ala Leu Leu Gly Ala Leu  
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His Ala Gln Ala Gln Asp Ser Thr Ser Asp Leu Ile Pro Ala Pro Pro  
 20 25 30

Leu Ser Lys Val Pro Leu Gln Gln Asn Phe Gln Asp Asn Gln Phe Gln  
 35 40 45

Gly Lys Trp Tyr Val Val Gly Leu Ala Gly Asn Ala Ile Leu Arg Glu  
 50 55 60

Asp Lys Asp Pro Gln Lys Met Tyr Ala Thr Ile Tyr Glu Leu Lys Glu  
 65 70 75 80

Asp Lys Ser Tyr Asn Val Thr Ser Val Leu Phe Arg Lys Lys Cys  
 85 90 95

Asp Tyr Trp Ile Arg Thr Phe Val Pro Gly Cys Gln Pro Gly Glu Phe  
 100 105 110

Thr Leu Gly Asn Ile Lys Ser Tyr Pro Gly Leu Thr Ser Tyr Leu Val  
 115 120 125

Arg Val Val Ser Thr Asn Tyr Asn Gln His Ala Met Val Phe Phe Lys  
 130 135 140

Lys Val Ser Gln Asn Arg Glu Tyr Phe Lys Ile Thr Leu Tyr Gly Arg  
 145 150 155 160

Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser  
 165 170 175

55/88

Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile  
180 185 190

Asp Gln Cys Ile Asp Gly  
195

<210> 27  
<211> 122  
<212> PRT  
<213> Homo sapiens

<400> 27  
Met Lys Leu Leu Thr Gly Leu Val Phe Cys Ser Leu Val Leu Gly Val  
1 5 10 15

Ser Ser Arg Ser Phe Phe Ser Phe Leu Gly Glu Ala Phe Asp Gly Ala  
20 25 30

Arg Asp Met Trp Arg Ala Tyr Ser Asp Met Arg Glu Ala Asn Tyr Ile  
35 40 45

Gly Ser Asp Lys Tyr Phe His Ala Arg Gly Asn Tyr Asp Ala Ala Lys  
50 55 60

Arg Gly Pro Gly Gly Val Trp Ala Ala Glu Ala Ile Ser Asp Ala Arg  
65 70 75 80

Glu Asn Ile Gln Arg Phe Phe Gly His Gly Ala Glu Asp Ser Leu Ala  
85 90 95

Asp Gln Ala Ala Asn Glu Trp Gly Arg Ser Gly Lys Asp Pro Asn His  
100 105 110

Phe Arg Pro Ala Gly Leu Pro Glu Lys Tyr  
115 120

<210> 28  
<211> 554  
<212> PRT  
<213> Homo sapiens

<400> 28  
Met Thr Ala Pro Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu  
1 5 10 15

Gly Ser Leu Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr  
20 25 30

Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu  
35 40 45

Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln  
50 55 60

Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys  
 65 70 75 80  
 Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr  
 85 90 95  
 Met Arg Phe Arg Asp Asn Thr Ala Asn Pro Ile Ala Ile Val Gln Leu  
 100 105 110  
 Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu  
 115 120 125  
 Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln  
 130 135 140  
 Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu  
 145 150 155 160  
 Asp Lys Asp Trp Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala  
 165 170 175  
 Glu Cys Ser Ser Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu  
 180 185 190  
 Tyr Pro Lys Ala Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His  
 195 200 205  
 Gln Pro Leu Ala Pro Ser Met Ala Pro Val Ala Gly Leu Thr Trp Glu  
 210 215 220  
 Asp Ser Glu Gly Thr Glu Gly Ser Ser Leu Leu Pro Gly Glu Gln Pro  
 225 230 235 240  
 Leu His Thr Val Asp Pro Gly Ser Ala Lys Gln Arg Pro Pro Arg Ser  
 245 250 255  
 Thr Cys Gln Ser Phe Glu Pro Pro Glu Thr Pro Val Val Lys Asp Ser  
 260 265 270  
 Thr Ile Gly Gly Ser Pro Gln Pro Arg Pro Ser Val Gly Ala Phe Asn  
 275 280 285  
 Pro Gly Met Glu Asp Ile Leu Asp Ser Ala Met Gly Thr Asn Trp Val  
 290 295 300  
 Pro Glu Glu Ala Ser Gly Glu Ala Ser Glu Ile Pro Val Pro Gln Gly  
 305 310 315 320  
 Thr Glu Leu Ser Pro Ser Arg Pro Gly Gly Ser Met Gln Thr Glu  
 325 330 335  
 Pro Ala Arg Pro Ser Asn Phe Leu Ser Ala Ser Ser Pro Leu Pro Ala  
 340 345 350  
 Ser Ala Lys Gly Gln Gln Pro Ala Asp Val Thr Ala Thr Ala Leu Pro  
 355 360 365

57/88

Arg Val Gly Pro Val Met Pro Thr Gly Gln Asp Trp Asn His Thr Pro  
 370 375 380  
 Gln Lys Thr Asp His Pro Ser Ala Leu Leu Arg Asp Pro Pro Glu Pro  
 385 390 395 400  
 Gly Ser Pro Arg Ile Ser Ser Leu Arg Pro Gln Ala Leu Ser Asn Pro  
 405 410 415  
 Ser Thr Leu Ser Ala Gln Pro Gln Leu Ser Arg Ser His Ser Ser Gly  
 420 425 430  
 Ser Val Leu Pro Leu Gly Glu Leu Glu Gly Arg Arg Ser Thr Arg Asp  
 435 440 445  
 Arg Thr Ser Pro Ala Glu Pro Glu Ala Ala Pro Ala Ser Glu Gly Ala  
 450 455 460  
 Ala Arg Pro Leu Pro Arg Phe Asn Ser Val Pro Leu Thr Asp Thr Gly  
 465 470 475 480  
 His Glu Arg Gln Ser Glu Gly Ser Ser Ser Pro Gln Leu Gln Glu Ser  
 485 490 495  
 Val Phe His Leu Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val  
 500 505 510  
 Gly Gly Leu Leu Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro  
 515 520 525  
 Gln Arg Ala Asp Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr  
 530 535 540  
 Gln Asp Asp Arg Gln Val Glu Leu Pro Val  
 545 550

<210> 29  
 <211> 107  
 <212> PRT  
 <213> Homo sapiens

<400> 29  
 Met Ala Arg Ala Ala Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu  
 1 5 10 15  
 Arg Val Ala Leu Leu Leu Leu Leu Val Ala Ala Gly Arg Arg Ala  
 20 25 30  
 Ala Gly Ala Ser Val Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr  
 35 40 45  
 Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys Ser  
 50 55 60  
 Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn  
 65 70 75 80

58/88

Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys Ile  
85 90 95

Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn  
100 105

<210> 30  
<211> 106  
<212> PRT  
<213> Homo sapiens

<400> 30  
Met Ala His Ala Thr Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu  
1 5 10 15

Arg Val Ala Leu Leu Leu Leu Leu Val Gly Ser Arg Arg Ala Ala  
20 25 30

Gly Ala Ser Val Val Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr Leu  
35 40 45

Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val Asn Val Arg Ser Pro  
50 55 60

Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn Gly  
65 70 75 80

Lys Lys Ala Cys Leu Asn Pro Ala Ser Pro Met Val Gln Lys Ile Ile  
85 90 95

Glu Lys Ile Leu Asn Lys Gly Ser Thr Asn  
100 105

<210> 31  
<211> 300  
<212> PRT  
<213> Homo sapiens

<400> 31  
Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala  
1 5 10 15

Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu  
20 25 30

Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro  
35 40 45

Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Thr Leu Pro Ser Lys Ser  
50 55 60

Asn Glu Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp  
65 70 75 80

Asp His Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp  
85 90 95

Val Asp Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser  
100 105 110

Asp Glu Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala  
115 120 125

Thr Glu Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly  
130 135 140

Arg Gly Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe  
145 150 155 160

Arg Arg Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu Asp Ile Thr  
165 170 175

Ser His Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro  
180 185 190

Val Ala Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys  
195 200 205

Asp Ser Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Thr His  
210 215 220

Ser His Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser  
225 230 235 240

Asn Glu His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser  
245 250 255

Arg Glu Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val  
260 265 270

Val Asp Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile  
275 280 285

Ser His Glu Leu Asp Ser Ala Ser Ser Glu Val Asn  
290 295 300

<210> 32  
<211> 295  
<212> PRT  
<213> Homo sapiens

<400> 32  
Met Glu His Gln Leu Leu Cys Cys Glu Val Glu Thr Ile Arg Arg Ala  
1 5 10 15

Tyr Pro Asp Ala Asn Leu Leu Asn Asp Arg Val Leu Arg Ala Met Leu  
20 25 30

60/88

Lys Ala Glu Glu Thr Cys Ala Pro Ser Val Ser Tyr Phe Lys Cys Val  
35 40 45

Gln Lys Glu Val Leu Pro Ser Met Arg Lys Ile Val Ala Thr Trp Met  
50 55 60

Leu Glu Val Cys Glu Glu Gln Lys Cys Glu Glu Glu Val Phe Pro Leu  
65 70 75 80

Ala Met Asn Tyr Leu Asp Arg Phe Leu Ser Leu Glu Pro Val Lys Lys  
85 90 95

Ser Arg Leu Gln Leu Leu Gly Ala Thr Cys Met Phe Val Ala Ser Lys  
100 105 110

Met Lys Glu Thr Ile Pro Leu Thr Ala Glu Lys Leu Cys Ile Tyr Thr  
115 120 125

Asp Gly Ser Ile Arg Pro Glu Glu Leu Leu Gln Met Glu Leu Leu Leu  
130 135 140

Val Asn Lys Leu Lys Trp Asn Leu Ala Ala Met Thr Pro His Asp Phe  
145 150 155 160

Ile Glu His Phe Leu Ser Lys Met Pro Glu Ala Glu Glu Asn Lys Gln  
165 170 175

Ile Ile Arg Lys His Ala Gln Thr Phe Val Ala Ser Cys Ala Thr Asp  
180 185 190

Val Lys Phe Ile Ser Asn Pro Pro Ser Met Val Ala Ala Gly Ser Val  
195 200 205

Val Ala Ala Val Gln Gly Leu Asn Leu Arg Ser Pro Asn Asn Phe Leu  
210 215 220

Ser Tyr Tyr Arg Leu Thr Arg Phe Leu Ser Arg Val Ile Lys Cys Asp  
225 230 235 240

Pro Asp Cys Leu Arg Ala Cys Gln Glu Gln Ile Glu Ala Leu Leu Glu  
245 250 255

Ser Ser Leu Arg Gln Ala Gln Gln Asn Met Asp Pro Lys Ala Ala Glu  
260 265 270

Glu Glu Glu Glu Glu Glu Glu Val Asp Leu Ala Cys Thr Pro Thr  
275 280 285

Asp Val Arg Asp Val Asp Ile  
290 295

<210> 33  
<211> 439  
<212> PRT  
<213> Homo sapiens

<400> 33  
Met Pro Leu Asn Val Ser Phe Thr Asn Arg Asn Tyr Asp Leu Asp Tyr  
1 5 10 15  
  
Asp Ser Val Gln Pro Tyr Phe Tyr Cys Asp Glu Glu Glu Asn Phe Tyr  
20 25 30  
  
Gln Gln Gln Gln Ser Glu Leu Gln Pro Pro Ala Pro Ser Glu Asp  
35 40 45  
  
Ile Trp Lys Lys Phe Glu Leu Leu Pro Thr Pro Pro Leu Ser Pro Ser  
50 55 60  
  
Arg Arg Ser Gly Leu Cys Ser Pro Ser Tyr Val Ala Val Thr Pro Phe  
65 70 75 80  
  
Ser Leu Arg Gly Asp Asn Asp Gly Gly Gly Ser Phe Ser Thr Ala  
85 90 95  
  
Asp Gln Leu Glu Met Val Thr Glu Leu Leu Gly Gly Asp Met Val Asn  
100 105 110  
  
Gln Ser Phe Ile Cys Asp Pro Asp Asp Glu Thr Phe Ile Lys Asn Ile  
115 120 125  
  
Ile Ile Gln Asp Cys Met Trp Ser Gly Phe Ser Ala Ala Ala Lys Leu  
130 135 140  
  
Val Ser Glu Lys Leu Ala Ser Tyr Gln Ala Ala Arg Lys Asp Ser Gly  
145 150 155 160  
  
Ser Pro Asn Pro Ala Arg Gly His Ser Val Cys Ser Thr Ser Ser Leu  
165 170 175  
  
Tyr Leu Gln Asp Leu Ser Ala Ala Ser Glu Cys Ile Asp Pro Ser  
180 185 190  
  
Val Val Phe Pro Tyr Pro Leu Asn Asp Ser Ser Ser Pro Lys Ser Cys  
195 200 205  
  
Ala Ser Gln Asp Ser Ser Ala Phe Ser Pro Ser Ser Asp Ser Leu Leu  
210 215 220  
  
Ser Ser Thr Glu Ser Ser Pro Gln Gly Ser Pro Glu Pro Leu Val Leu  
225 230 235 240  
  
His Glu Glu Thr Pro Pro Thr Thr Ser Ser Asp Ser Glu Glu Glu Gln  
245 250 255  
  
Glu Asp Glu Glu Glu Ile Asp Val Val Ser Val Glu Lys Arg Gln Ala  
260 265 270  
  
Pro Gly Lys Arg Ser Glu Ser Gly Ser Pro Ser Ala Gly Gly His Ser  
275 280 285  
  
Lys Pro Pro His Ser Pro Leu Val Leu Lys Arg Cys His Val Ser Thr  
290 295 300

62/88

His Gln His Asn Tyr Ala Ala Pro Pro Ser Thr Arg Lys Asp Tyr Pro  
 305 310 315 320  
 Ala Ala Lys Arg Val Lys Leu Asp Ser Val Arg Val Leu Arg Gln Ile  
 325 330 335  
 Ser Asn Asn Arg Lys Cys Thr Ser Pro Arg Ser Ser Asp Thr Glu Glu  
 340 345 350  
 Asn Val Lys Arg Arg Thr His Asn Val Leu Glu Arg Gln Arg Arg Asn  
 355 360 365  
 Glu Leu Lys Arg Ser Phe Phe Ala Leu Arg Asp Gln Ile Pro Glu Leu  
 370 375 380  
 Glu Asn Asn Glu Lys Ala Pro Lys Val Val Ile Leu Lys Lys Ala Thr  
 385 390 395 400  
 Ala Tyr Ile Leu Ser Val Gln Ala Glu Glu Gln Lys Leu Ile Ser Glu  
 405 410 415  
 Glu Asp Leu Leu Arg Lys Arg Arg Glu Gln Leu Lys His Lys Leu Glu  
 420 425 430  
 Gln Leu Arg Asn Ser Cys Ala  
 435

<210> 34  
 <211> 164  
 <212> PRT  
 <213> Homo sapiens

<400> 34  
 Met Ser Glu Pro Ala Gly Asp Val Arg Gln Asn Pro Cys Gly Ser Lys  
 1 5 10 15  
 Ala Cys Arg Arg Leu Phe Gly Pro Val Asp Ser Glu Gln Leu Ser Arg  
 20 25 30  
 Asp Cys Asp Ala Leu Met Ala Gly Cys Ile Gln Glu Ala Arg Glu Arg  
 35 40 45  
 Trp Asn Phe Asp Phe Val Thr Glu Thr Pro Leu Glu Gly Asp Phe Ala  
 50 55 60  
 Trp Glu Arg Val Arg Gly Leu Gly Leu Pro Lys Leu Tyr Leu Pro Thr  
 65 70 75 80  
 Gly Pro Arg Arg Gly Arg Asp Glu Leu Gly Gly Arg Arg Pro Gly  
 85 90 95  
 Thr Ser Pro Ala Leu Leu Gln Gly Thr Ala Glu Glu Asp His Val Asp  
 100 105 110  
 Leu Ser Leu Ser Cys Thr Leu Val Pro Arg Ser Gly Glu Gln Ala Glu  
 115 120 125

63/88

Gly Ser Pro Gly Gly Pro Gly Asp Ser Gln Gly Arg Lys Arg Arg Gln  
130 135 140  
Thr Ser Met Thr Asp Phe Tyr His Ser Lys Arg Arg Leu Ile Phe Ser  
145 150 155 160  
Lys Arg Lys Pro

<210> 35  
<211> 105  
<212> PRT  
<213> Homo sapiens

<400> 35  
Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu Leu His Gly  
1 5 10 15  
Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu Thr Arg Pro Val His  
20 25 30  
Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val Val Leu His Arg  
35 40 45  
Ala Gly Ala Arg Leu Asp Val Arg Asp Ala Trp Gly Arg Leu Pro Val  
50 55 60  
Asp Leu Ala Glu Glu Leu Gly His Arg Asp Val Ala Arg Tyr Leu Arg  
65 70 75 80  
Ala Ala Ala Gly Gly Thr Arg Gly Ser Asn His Ala Arg Ile Asp Ala  
85 90 95  
Ala Glu Gly Pro Ser Asp Ile Pro Asp  
100 105

<210> 36  
<211> 173  
<212> PRT  
<213> Homo sapiens

<400> 36  
Met Gly Arg Gly Arg Cys Val Gly Pro Ser Leu Gln Leu Arg Gly Gln  
1 5 10 15  
Glu Trp Arg Cys Ser Pro Leu Val Pro Lys Gly Gly Ala Ala Ala Ala  
20 25 30  
Glu Leu Gly Pro Gly Gly Glu Asn Met Val Arg Arg Phe Leu Val  
35 40 45  
Thr Leu Arg Ile Arg Arg Ala Cys Gly Pro Pro Arg Val Arg Val Phe  
50 55 60

64/88

Val Val His Ile Pro Arg Leu Thr Gly Glu Trp Ala Ala Pro Gly Ala  
 65 70 75 80

Pro Ala Ala Val Ala Leu Val Leu Met Leu Leu Arg Ser Gln Arg Leu  
 85 90 95

Gly Gln Gln Pro Leu Pro Arg Arg Pro Gly His Asp Asp Gly Gln Arg  
 100 105 110

Pro Ser Gly Gly Ala Ala Ala Pro Arg Arg Gly Ala Gln Leu Arg  
 115 120 125

Arg Pro Arg His Ser His Pro Thr Arg Ala Arg Arg Cys Pro Gly Gly  
 130 135 140

Leu Pro Gly His Ala Gly Gly Ala Ala Pro Gly Arg Gly Ala Ala Gly  
 145 150 155 160

Arg Ala Arg Cys Leu Gly Pro Ser Ala Arg Gly Pro Gly  
 165 170

<210> 37  
 <211> 468  
 <212> PRT  
 <213> Homo sapiens

<400> 37  
 Met Val Asp Thr Glu Ser Pro Leu Cys Pro Leu Ser Pro Leu Glu Ala  
 1 5 10 15

Gly Asp Leu Glu Ser Pro Leu Ser Glu Glu Phe Leu Gln Glu Met Gly  
 20 25 30

Asn Ile Gln Glu Ile Ser Gln Ser Ile Gly Glu Asp Ser Ser Gly Ser  
 35 40 45

Phe Gly Phe Thr Glu Tyr Gln Tyr Leu Gly Ser Cys Pro Gly Ser Asp  
 50 55 60

Gly Ser Val Ile Thr Asp Thr Leu Ser Pro Ala Ser Ser Pro Ser Ser  
 65 70 75 80

Val Thr Tyr Pro Val Val Pro Gly Ser Val Asp Glu Ser Pro Ser Gly  
 85 90 95

Ala Leu Asn Ile Glu Cys Arg Ile Cys Gly Asp Lys Ala Ser Gly Tyr  
 100 105 110

His Tyr Gly Val His Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg  
 115 120 125

Thr Ile Arg Leu Lys Leu Val Tyr Asp Lys Cys Asp Arg Ser Cys Lys  
 130 135 140

Ile Gln Lys Lys Asn Arg Asn Lys Cys Gln Tyr Cys Arg Phe His Lys  
 145 150 155 160

Cys Leu Ser Val Gly Met Ser His Asn Ala Ile Arg Phe Gly Arg Met  
165 170 175

Pro Arg Ser Glu Lys Ala Lys Leu Lys Ala Glu Ile Leu Thr Cys Glu  
180 185 190

His Asp Ile Glu Asp Ser Glu Thr Ala Asp Leu Lys Ser Leu Ala Lys  
195 200 205

Arg Ile Tyr Glu Ala Tyr Leu Lys Asn Phe Asn Met Asn Lys Val Lys  
210 215 220

Ala Arg Val Ile Leu Ser Gly Lys Ala Ser Asn Asn Pro Pro Phe Val  
225 230 235 240

Ile His Asp Met Glu Thr Leu Cys Met Ala Glu Lys Thr Leu Val Ala  
245 250 255

Lys Leu Val Ala Asn Gly Ile Gln Asn Lys Glu Ala Glu Val Arg Ile  
260 265 270

Phe His Cys Cys Gln Cys Thr Ser Val Glu Thr Val Thr Glu Leu Thr  
275 280 285

Glu Phe Ala Lys Ala Ile Pro Gly Phe Ala Asn Leu Asp Leu Asn Asp  
290 295 300

Gln Val Thr Leu Leu Lys Tyr Gly Val Tyr Glu Ala Ile Phe Ala Met  
305 310 315 320

Leu Ser Ser Val Met Asn Lys Asp Gly Met Leu Val Ala Tyr Gly Asn  
325 330 335

Gly Phe Ile Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Cys  
340 345 350

Asp Ile Met Glu Pro Lys Phe Asp Phe Ala Met Lys Phe Asn Ala Leu  
355 360 365

Glu Leu Asp Asp Ser Asp Ile Ser Leu Phe Val Ala Ala Ile Ile Cys  
370 375 380

Cys Gly Asp Arg Pro Gly Leu Leu Asn Val Gly His Ile Glu Lys Met  
385 390 395 400

Gln Glu Gly Ile Val His Val Leu Arg Leu His Leu Gln Ser Asn His  
405 410 415

Pro Asp Asp Ile Phe Leu Phe Pro Lys Leu Leu Gln Lys Met Ala Asp  
420 425 430

Leu Arg Gln Leu Val Thr Glu His Ala Gln Leu Val Gln Ile Ile Lys  
435 440 445

66/88

Lys Thr Glu Ser Asp Ala Ala Leu His Pro Leu Leu Gln Glu Ile Tyr  
 450 455 460

Arg Asp Met Tyr  
 465

<210> 38  
 <211> 505  
 <212> PRT  
 <213> Homo sapiens

<400> 38  
 Met Gly Glu Thr Leu Gly Asp Ser Pro Ile Asp Pro Glu Ser Asp Ser  
 1 5 10 15

Phe Thr Asp Thr Leu Ser Ala Asn Ile Ser Gln Glu Met Thr Met Val  
 20 25 30

Asp Thr Glu Met Pro Phe Trp Pro Thr Asn Phe Gly Ile Ser Ser Val  
 35 40 45

Asp Leu Ser Val Met Glu Asp His Ser His Ser Phe Asp Ile Lys Pro  
 50 55 60

Phe Thr Thr Val Asp Phe Ser Ser Ile Ser Thr Pro His Tyr Glu Asp  
 65 70 75 80

Ile Pro Phe Thr Arg Thr Asp Pro Val Val Ala Asp Tyr Lys Tyr Asp  
 85 90 95

Leu Lys Leu Gln Glu Tyr Gln Ser Ala Ile Lys Val Glu Pro Ala Ser  
 100 105 110

Pro Pro Tyr Tyr Ser Glu Lys Thr Gln Leu Tyr Asn Lys Pro His Glu  
 115 120 125

Glu Pro Ser Asn Ser Leu Met Ala Ile Glu Cys Arg Val Cys Gly Asp  
 130 135 140

Lys Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly Cys Lys  
 145 150 155 160

Gly Phe Phe Arg Arg Thr Ile Arg Leu Lys Leu Ile Tyr Asp Arg Cys  
 165 170 175

Asp Leu Asn Cys Arg Ile His Lys Lys Ser Arg Asn Lys Cys Gln Tyr  
 180 185 190

Cys Arg Phe Gln Lys Cys Leu Ala Val Gly Met Ser His Asn Ala Ile  
 195 200 205

Arg Phe Gly Arg Met Pro Gln Ala Glu Lys Glu Lys Leu Leu Ala Glu  
 210 215 220

Ile Ser Ser Asp Ile Asp Gln Leu Asn Pro Glu Ser Ala Asp Leu Arg  
 225 230 235 240

67/88

Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu  
245 250 255

Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys  
260 265 270

Ser Pro Phe Val Ile Tyr Asp Met Asn Ser Leu Met Met Gly Glu Asp  
275 280 285

Lys Ile Lys Phe Lys His Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu  
290 295 300

Val Ala Ile Arg Ile Phe Gln Gly Cys Gln Phe Arg Ser Val Glu Ala  
305 310 315 320

Val Gln Glu Ile Thr Glu Tyr Ala Lys Ser Ile Pro Gly Phe Val Asn  
325 330 335

Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val His Glu  
340 345 350

Ile Ile Tyr Thr Met Leu Ala Ser Leu Met Asn Lys Asp Gly Val Leu  
355 360 365

Ile Ser Glu Gly Gln Gly Phe Met Thr Arg Glu Phe Leu Lys Ser Leu  
370 375 380

Arg Lys Pro Phe Gly Asp Phe Met Glu Pro Lys Phe Glu Phe Ala Val  
385 390 395 400

Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile  
405 410 415

Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly Leu Leu Asn Val Lys  
420 425 430

Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln  
435 440 445

Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu  
450 455 460

Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr Glu His Val Gln Leu  
465 470 475 480

Leu Gln Val Ile Lys Lys Thr Glu Thr Asp Met Ser Leu His Pro Leu  
485 490 495

Leu Gln Glu Ile Tyr Lys Asp Leu Tyr  
500 505

<210> 39  
<211> 441  
<212> PRT  
<213> Homo sapiens

68/88

<400> 39  
Met Glu Gln Pro Gln Glu Glu Ala Pro Glu Val Arg Glu Glu Glu Glu  
1 5 10 15  
Lys Glu Glu Val Ala Glu Ala Glu Gly Ala Pro Glu Leu Asn Gly Gly  
20 25 30  
Pro Gln His Ala Leu Pro Ser Ser Ser Tyr Thr Asp Leu Ser Arg Ser  
35 40 45  
Ser Ser Pro Pro Ser Leu Leu Asp Gln Leu Gln Met Gly Cys Asp Gly  
50 55 60  
Ala Ser Cys Gly Ser Leu Asn Met Glu Cys Arg Val Cys Gly Asp Lys  
65 70 75 80  
Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly Cys Lys Gly  
85 90 95  
Phe Phe Arg Arg Thr Ile Arg Met Lys Leu Glu Tyr Glu Lys Cys Glu  
100 105 110  
Arg Ser Cys Lys Ile Gln Lys Lys Asn Arg Asn Lys Cys Gln Tyr Cys  
115 120 125  
Arg Phe Gln Lys Cys Leu Ala Leu Gly Met Ser His Asn Ala Ile Arg  
130 135 140  
Phe Gly Arg Met Pro Glu Ala Glu Lys Arg Lys Leu Val Ala Gly Leu  
145 150 155 160  
Thr Ala Asn Glu Gly Ser Gln Tyr Asn Pro Gln Val Ala Asp Leu Lys  
165 170 175  
Ala Phe Ser Lys His Ile Tyr Asn Ala Tyr Leu Lys Asn Phe Asn Met  
180 185 190  
Thr Lys Lys Lys Ala Arg Ser Ile Leu Thr Gly Lys Ala Ser His Thr  
195 200 205  
Ala Pro Phe Val Ile His Asp Ile Glu Thr Leu Trp Gln Ala Glu Lys  
210 215 220  
Gly Leu Val Trp Lys Gln Leu Val Asn Gly Leu Pro Pro Tyr Lys Glu  
225 230 235 240  
Ile Ser Val His Val Phe Tyr Arg Cys Gln Cys Thr Thr Val Glu Thr  
245 250 255  
Val Arg Glu Leu Thr Glu Phe Ala Lys Ser Ile Pro Ser Phe Ser Ser  
260 265 270  
Leu Phe Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val His Glu  
275 280 285  
Ala Ile Phe Ala Met Leu Ala Ser Ile Val Asn Lys Asp Gly Leu Leu  
290 295 300

69/88

Val Ala Asn Gly Ser Gly Phe Val Thr Arg Glu Phe Leu Arg Ser Leu  
 305 310 315 320  
 Arg Lys Pro Phe Ser Asp Ile Ile Glu Pro Lys Phe Glu Phe Ala Val  
 325 330 335  
 Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Leu Phe Ile  
 340 345 350  
 Ala Ala Ile Ile Leu Cys Gly Asp Arg Pro Gly Leu Met Asn Val Pro  
 355 360 365  
 Arg Val Glu Ala Ile Gln Asp Thr Ile Leu Arg Ala Leu Glu Phe His  
 370 375 380  
 Leu Gln Ala Asn His Pro Asp Ala Gln Tyr Leu Phe Pro Lys Leu Leu  
 385 390 395 400  
 Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu His Ala Gln Met  
 405 410 415  
 Met Gln Arg Ile Lys Lys Thr Glu Thr Glu Thr Ser Leu His Pro Leu  
 420 425 430  
 Leu Gln Glu Ile Tyr Lys Asp Met Tyr  
 435 440

<210> 40  
 <211> 742  
 <212> PRT  
 <213> Homo sapiens

<400> 40  
 Met Asp Lys Phe Trp Trp His Ala Ala Trp Gly Leu Cys Leu Val Pro  
 1 5 10 15  
 Leu Ser Leu Ala Gln Ile Asp Leu Asn Ile Thr Cys Arg Phe Ala Gly  
 20 25 30  
 Val Phe His Val Glu Lys Asn Gly Arg Tyr Ser Ile Ser Arg Thr Glu  
 35 40 45  
 Ala Ala Asp Leu Cys Lys Ala Phe Asn Ser Thr Leu Pro Thr Met Ala  
 50 55 60  
 Gln Met Glu Lys Ala Leu Ser Ile Gly Phe Glu Thr Cys Arg Tyr Gly  
 65 70 75 80  
 Phe Ile Glu Gly His Val Val Ile Pro Arg Ile His Pro Asn Ser Ile  
 85 90 95  
 Cys Ala Ala Asn Asn Thr Gly Val Tyr Ile Leu Thr Ser Asn Thr Ser  
 100 105 110

70/88

Gln Tyr Asp Thr Tyr Cys Phe Asn Ala Ser Ala Pro Pro Glu Glu Asp  
115 120 125

Cys Thr Ser Val Thr Asp Leu Pro Asn Ala Phe Asp Gly Pro Ile Thr  
130 135 140

Ile Thr Ile Val Asn Arg Asp Gly Thr Arg Tyr Val Gln Lys Gly Glu  
145 150 155 160

Tyr Arg Thr Asn Pro Glu Asp Ile Tyr Pro Ser Asn Pro Thr Asp Asp  
165 170 175

Asp Val Ser Ser Gly Ser Ser Ser Glu Arg Ser Ser Thr Ser Gly Gly  
180 185 190

Tyr Ile Phe Tyr Thr Phe Ser Thr Val His Pro Ile Pro Asp Glu Asp  
195 200 205

Ser Pro Trp Ile Thr Asp Ser Thr Asp Arg Ile Pro Ala Thr Thr Leu  
210 215 220

Met Ser Thr Ser Ala Thr Ala Thr Glu Thr Ala Thr Lys Arg Gln Glu  
225 230 235 240

Thr Trp Asp Trp Phe Ser Trp Leu Phe Leu Pro Ser Glu Ser Lys Asn  
245 250 255

His Leu His Thr Thr Thr Gln Met Ala Gly Thr Ser Ser Asn Thr Ile  
260 265 270

Ser Ala Gly Trp Glu Pro Asn Glu Glu Asn Glu Asp Glu Arg Asp Arg  
275 280 285

His Leu Ser Phe Ser Gly Ser Gly Ile Asp Asp Asp Glu Asp Phe Ile  
290 295 300

Ser Ser Thr Ile Ser Thr Thr Pro Arg Ala Phe Asp His Thr Lys Gln  
305 310 315 320

Asn Gln Asp Trp Thr Gln Trp Asn Pro Ser His Ser Asn Pro Glu Val  
325 330 335

Leu Leu Gln Thr Thr Arg Met Thr Asp Val Asp Arg Asn Gly Thr  
340 345 350

Thr Ala Tyr Glu Gly Asn Trp Asn Pro Glu Ala His Pro Pro Leu Ile  
355 360 365

His His Glu His His Glu Glu Glu Glu Thr Pro His Ser Thr Ser Thr  
370 375 380

Ile Gln Ala Thr Pro Ser Ser Thr Thr Glu Glu Thr Ala Thr Gln Lys  
385 390 395 400

Glu Gln Trp Phe Gly Asn Arg Trp His Glu Gly Tyr Arg Gln Thr Pro  
405 410 415

71/88

Lys Glu Asp Ser His Ser Thr Thr Gly Thr Ala Ala Ala Ser Ala His  
420 425 430

Thr Ser His Pro Met Gln Gly Arg Thr Thr Pro Ser Pro Glu Asp Ser  
435 440 445

Ser Trp Thr Asp Phe Phe Asn Pro Ile Ser His Pro Met Gly Arg Gly  
450 455 460

His Gln Ala Gly Arg Arg Met Asp Met Asp Ser Ser His Ser Ile Thr  
465 470 475 480

Leu Gln Pro Thr Ala Asn Pro Asn Thr Gly Leu Val Glu Asp Leu Asp  
485 490 495

Arg Thr Gly Pro Leu Ser Met Thr Thr Gln Gln Ser Asn Ser Gln Ser  
500 505 510

Phe Ser Thr Ser His Glu Gly Leu Glu Glu Asp Lys Asp His Pro Thr  
515 520 525

Thr Ser Thr Leu Thr Ser Ser Asn Arg Asn Asp Val Thr Gly Gly Arg  
530 535 540

Arg Asp Pro Asn His Ser Glu Gly Ser Thr Thr Leu Leu Glu Gly Tyr  
545 550 555 560

Thr Ser His Tyr Pro His Thr Lys Glu Ser Arg Thr Phe Ile Pro Val  
565 570 575

Thr Ser Ala Lys Thr Gly Ser Phe Gly Val Thr Ala Val Thr Val Gly  
580 585 590

Asp Ser Asn Ser Asn Val Asn Arg Ser Leu Ser Gly Asp Gln Asp Thr  
595 600 605

Phe His Pro Ser Gly Gly Ser His Thr Thr His Gly Ser Glu Ser Asp  
610 615 620

Gly His Ser His Gly Ser Gln Glu Gly Gly Ala Asn Thr Thr Ser Gly  
625 630 635 640

Pro Ile Arg Thr Pro Gln Ile Pro Glu Trp Leu Ile Ile Leu Ala Ser  
645 650 655

Leu Leu Ala Leu Ala Leu Ile Leu Ala Val Cys Ile Ala Val Asn Ser  
660 665 670

Arg Arg Arg Cys Gly Gln Lys Lys Lys Leu Val Ile Asn Ser Gly Asn  
675 680 685

Gly Ala Val Glu Asp Arg Lys Pro Ser Gly Leu Asn Gly Glu Ala Ser  
690 695 700

Lys Ser Gln Glu Met Val His Leu Val Asn Lys Glu Ser Ser Glu Thr  
705 710 715 720

72/88

Pro Asp Gln Phe Met Thr Ala Asp Glu Thr Arg Asn Leu Gln Asn Val  
 725 730 735

Asp Met Lys Ile Gly Val  
 740

<210> 41  
 <211> 489  
 <212> PRT  
 <213> Homo sapiens

<400> 41  
 Met Leu Met Arg Leu Val Leu Thr Val Arg Ser Asn Leu Ile Pro Ser  
 1 5 10 15

Pro Pro Thr Tyr Asn Ser Ala His Asp Tyr Ile Ser Trp Glu Ser Phe  
 20 25 30

Ser Asn Val Ser Tyr Tyr Thr Arg Ile Leu Pro Ser Val Pro Lys Asp  
 35 40 45

Cys Pro Thr Pro Met Gly Thr Lys Gly Lys Lys Gln Leu Pro Asp Ala  
 50 55 60

Gln Leu Leu Ala Arg Arg Phe Leu Leu Arg Arg Lys Phe Ile Pro Asp  
 65 70 75 80

Pro Gln Gly Thr Asn Leu Met Phe Ala Phe Phe Ala Gln His Phe Thr  
 85 90 95

His Gln Phe Phe Lys Thr Ser Gly Lys Met Gly Pro Gly Phe Thr Lys  
 100 105 110

Ala Leu Gly His Gly Val Asp Leu Gly His Ile Tyr Gly Asp Asn Leu  
 115 120 125

Glu Arg Gln Tyr Gln Leu Arg Leu Phe Lys Asp Gly Lys Leu Lys Tyr  
 130 135 140

Gln Val Leu Asp Gly Glu Met Tyr Pro Pro Ser Val Glu Glu Ala Pro  
 145 150 155 160

Val Leu Met His Tyr Pro Arg Gly Ile Pro Pro Gln Ser Gln Met Ala  
 165 170 175

Val Gly Gln Glu Val Phe Gly Leu Leu Pro Gly Leu Met Leu Tyr Ala  
 180 185 190

Thr Leu Trp Leu Arg Glu His Asn Arg Val Cys Asp Leu Leu Lys Ala  
 195 200 205

Glu His Pro Thr Trp Gly Asp Glu Gln Leu Phe Gln Thr Thr Arg Leu  
 210 215 220

Ile Leu Ile Gly Glu Thr Ile Lys Ile Val Ile Glu Glu Tyr Val Gln  
 225 230 235 240

73/88

Gln Leu Ser Gly Tyr Phe Leu Gln Leu Lys Phe Asp Pro Glu Leu Leu  
 245 250 255  
 Phe Gly Val Gln Phe Gln Tyr Arg Asn Arg Ile Ala Met Glu Phe Asn  
 260 265 270  
 His Leu Tyr His Trp His Pro Leu Met Pro Asp Ser Phe Lys Val Gly  
 275 280 285  
 Ser Gln Glu Tyr Ser Tyr Glu Gln Phe Leu Phe Asn Thr Ser Met Leu  
 290 295 300  
 Val Asp Tyr Gly Val Glu Ala Leu Val Asp Ala Phe Ser Arg Gln Ile  
 305 310 315 320  
 Ala Gly Arg Ile Gly Gly Arg Asn Met Asp His His Ile Leu His  
 325 330 335  
 Val Ala Val Asp Val Ile Arg Glu Ser Arg Glu Met Arg Leu Gln Pro  
 340 345 350  
 Phe Asn Glu Tyr Arg Lys Arg Phe Gly Met Lys Pro Tyr Thr Ser Phe  
 355 360 365  
 Gln Glu Leu Val Gly Glu Lys Glu Met Ala Ala Glu Leu Glu Leu  
 370 375 380  
 Tyr Gly Asp Ile Asp Ala Leu Glu Phe Tyr Pro Gly Leu Leu Leu Glu  
 385 390 395 400  
 Lys Cys His Pro Asn Ser Ile Phe Gly Glu Ser Met Ile Glu Ile Gly  
 405 410 415  
 Ala Pro Phe Ser Leu Lys Gly Leu Leu Gly Asn Pro Ile Cys Ser Pro  
 420 425 430  
 Glu Tyr Trp Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Asn Ile  
 435 440 445  
 Val Lys Thr Ala Thr Leu Lys Lys Leu Val Cys Leu Asn Thr Lys Thr  
 450 455 460  
 Cys Pro Tyr Val Ser Phe Arg Val Pro Asp Ala Ser Gln Asp Asp Gly  
 465 470 475 480  
 Pro Ala Val Glu Arg Pro Ser Thr Glu  
 485

<210> 42  
 <211> 96  
 <212> PRT  
 <213> Homo sapiens

<400> 42  
 Met Ser Glu Ser Ser Ser Lys Ser Ser Gln Pro Leu Ala Ser Lys Gln  
 1 5 10 15

Glu Lys Asp Gly Thr Glu Lys Arg Gly Arg Gly Arg Pro Arg Lys Gln  
20 25 30

Pro Pro Lys Glu Pro Ser Glu Val Pro Thr Pro Lys Arg Pro Arg Gly  
35 40 45

Arg Pro Lys Gly Ser Lys Asn Lys Gly Ala Ala Lys Thr Arg Lys Thr  
50 55 60

Thr Thr Thr Pro Gly Arg Lys Pro Arg Gly Arg Pro Lys Lys Leu Glu  
65 70 75 80

Lys Glu Glu Glu Glu Gly Ile Ser Gln Glu Ser Ser Glu Glu Glu Gln  
85 90 95

<210> 43  
<211> 79  
<212> PRT  
<213> Homo sapiens

<400> 43  
Met Ala His Lys Gln Ile Tyr Tyr Ser Asp Lys Tyr Phe Asp Glu His  
1 5 10 15

Tyr Glu Tyr Arg His Val Met Leu Pro Arg Glu Leu Ser Lys Gln Val  
20 25 30

Pro Lys Thr His Leu Met Ser Glu Glu Glu Trp Arg Arg Leu Gly Val  
35 40 45

Gln Gln Ser Leu Gly Trp Val His Tyr Met Ile His Glu Pro Glu Pro  
50 55 60

His Ile Leu Leu Phe Arg Arg Pro Leu Pro Lys Asp Gln Gln Lys  
65 70 75

<210> 44  
<211> 885  
<212> PRT  
<213> Homo sapiens

<400> 44  
Met Val Leu Ser Gly Cys Ala Ile Ile Val Arg Gly Gln Pro Arg Gly  
1 5 10 15

Gly Pro Pro Pro Glu Arg Gln Ile Asn Leu Ser Asn Ile Arg Ala Gly  
20 25 30

Asn Leu Ala Arg Arg Ala Ala Ala Thr Gln Pro Asp Ala Lys Asp Thr  
35 40 45

Pro Asp Glu Pro Trp Ala Phe Pro Ala Arg Glu Phe Leu Arg Lys Lys  
50 55 60

75/88

Leu Ile Gly Lys Glu Val Cys Phe Thr Ile Glu Asn Lys Thr Pro Gln  
65 70 75 80

Gly Arg Glu Tyr Gly Met Ile Tyr Leu Gly Lys Asp Thr Asn Gly Glu  
85 90 95

Asn Ile Ala Glu Ser Leu Val Ala Glu Gly Leu Ala Thr Arg Arg Glu  
100 105 110

Gly Met Arg Ala Asn Asn Pro Glu Gln Asn Arg Leu Ser Glu Cys Glu  
115 120 125

Glu Gln Ala Lys Ala Ala Lys Lys Gly Met Trp Ser Glu Gly Asn Gly  
130 135 140

Ser His Thr Ile Arg Asp Leu Lys Tyr Thr Ile Glu Asn Pro Arg His  
145 150 155 160

Phe Val Asp Ser His His Gln Lys Pro Val Asn Ala Ile Ile Glu His  
165 170 175

Val Arg Asp Gly Ser Val Val Arg Ala Leu Leu Leu Pro Asp Tyr Tyr  
180 185 190

Leu Val Thr Val Met Leu Ser Gly Ile Lys Cys Pro Thr Phe Arg Arg  
195 200 205

Glu Ala Asp Gly Ser Glu Thr Pro Glu Pro Phe Ala Ala Glu Ala Lys  
210 215 220

Phe Phe Thr Glu Ser Arg Leu Leu Gln Arg Asp Val Gln Ile Ile Leu  
225 230 235 240

Glu Ser Cys His Asn Gln Asn Ile Val Gly Thr Ile Leu His Pro Asn  
245 250 255

Gly Asn Ile Thr Glu Leu Leu Leu Lys Glu Gly Phe Ala Arg Cys Val  
260 265 270

Asp Trp Ser Ile Ala Val Tyr Thr Arg Gly Ala Glu Lys Leu Arg Ala  
275 280 285

Ala Glu Arg Phe Ala Lys Glu Arg Arg Leu Arg Ile Trp Arg Asp Tyr  
290 295 300

Val Ala Pro Thr Ala Asn Leu Asp Gln Lys Asp Lys Gln Phe Val Ala  
305 310 315 320

Lys Val Met Gln Val Leu Asn Ala Asp Ala Ile Val Val Lys Leu Asn  
325 330 335

Ser Gly Asp Tyr Lys Thr Ile His Leu Ser Ser Ile Arg Pro Pro Arg  
340 345 350

Leu Glu Gly Glu Asn Thr Gln Asp Lys Asn Lys Lys Leu Arg Pro Leu  
355 360 365

76/88

Tyr Asp Ile Pro Tyr Met Phe Glu Ala Arg Glu Phe Leu Arg Lys Lys  
370 375 380

Leu Ile Gly Lys Lys Val Asn Val Thr Val Asp Tyr Ile Arg Pro Ala  
385 390 395 400

Ser Pro Ala Thr Glu Thr Val Pro Ala Phe Ser Glu Arg Thr Cys Ala  
405 410 415

Thr Val Thr Ile Gly Gly Ile Asn Ile Ala Glu Ala Leu Val Ser Lys  
420 425 430

Gly Leu Ala Thr Val Ile Arg Tyr Arg Gln Asp Asp Asp Gln Arg Ser  
435 440 445

Ser His Tyr Asp Glu Leu Leu Ala Ala Glu Ala Arg Ala Ile Lys Asn  
450 455 460

Gly Lys Gly Leu His Ser Lys Lys Glu Val Pro Ile His Arg Val Ala  
465 470 475 480

Asp Ile Ser Gly Asp Thr Gln Lys Ala Lys Gln Phe Leu Pro Phe Leu  
485 490 495

Gln Arg Ala Gly Arg Ser Glu Ala Val Val Glu Tyr Val Phe Ser Gly  
500 505 510

Ser Arg Leu Lys Leu Tyr Leu Pro Lys Glu Thr Cys Leu Ile Thr Phe  
515 520 525

Leu Leu Ala Gly Ile Glu Cys Pro Arg Gly Ala Arg Asn Leu Pro Gly  
530 535 540

Leu Val Gln Glu Gly Glu Pro Phe Ser Glu Glu Ala Thr Leu Phe Thr  
545 550 555 560

Lys Glu Leu Val Leu Gln Arg Glu Val Glu Val Glu Val Glu Ser Met  
565 570 575

Asp Lys Ala Gly Asn Phe Ile Gly Trp Leu His Ile Asp Gly Ala Asn  
580 585 590

Leu Ser Val Leu Leu Val Glu His Ala Leu Ser Lys Val His Phe Thr  
595 600 605

Ala Glu Arg Ser Ser Tyr Tyr Lys Ser Leu Leu Ser Ala Glu Glu Ala  
610 615 620

Ala Lys Gln Lys Lys Glu Lys Val Trp Ala His Tyr Glu Glu Gln Pro  
625 630 635 640

Val Glu Glu Val Met Pro Val Leu Glu Glu Lys Glu Arg Ser Ala Ser  
645 650 655

Tyr Lys Pro Val Phe Val Thr Glu Ile Thr Asp Asp Leu His Phe Tyr  
660 665 670

77/88

Val Gln Asp Val Glu Thr Gly Thr Gln Phe Gln Lys Leu Met Glu Asn  
675 680 685

Met Arg Asn Asp Ile Ala Ser His Pro Pro Val Glu Gly Ser Tyr Ala  
690 695 700

Pro Arg Arg Gly Glu Phe Cys Ile Ala Lys Phe Val Asp Gly Glu Trp  
705 710 715 720

Tyr Arg Ala Arg Val Glu Lys Val Glu Ser Pro Ala Lys Ile His Val  
725 730 735

Phe Tyr Ile Asp Tyr Gly Asn Arg Glu Val Leu Pro Ser Thr Arg Leu  
740 745 750

Gly Thr Leu Ser Pro Ala Phe Ser Thr Arg Val Leu Pro Ala Gln Ala  
755 760 765

Thr Glu Tyr Ala Phe Ala Phe Ile Gln Val Pro Gln Asp Asp Asp Ala  
770 775 780

Arg Thr Asp Ala Val Asp Ser Val Val Arg Asp Ile Gln Asn Thr Gln  
785 790 795 800

Cys Leu Leu Asn Val Glu His Leu Ser Ala Gly Cys Pro His Val Thr  
805 810 815

Leu Gln Phe Ala Asp Ser Lys Gly Asp Val Gly Leu Gly Leu Val Lys  
820 825 830

Glu Gly Leu Val Met Val Glu Val Arg Lys Glu Lys Gln Phe Gln Lys  
835 840 845

Val Ile Thr Glu Tyr Leu Asn Ala Gln Glu Ser Ala Lys Ser Ala Arg  
850 855 860

Leu Asn Leu Trp Arg Tyr Gly Asp Phe Arg Ala Asp Asp Ala Asp Glu  
865 870 875 880

Phe Gly Tyr Ser Arg  
885

<210> 45  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 45  
agatattgca cgggagaata tacaaa

78/88

<210> 46  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 46  
tcaattcctg aaattaaagt tcggata

27

<210> 47  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 47  
tctgcagagt tggaagcact cta

23

<210> 48  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 48  
gccgaggctt ttctaccaga a

21

<210> 49  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 49  
catggcttga tcagcaagga

20

79/88

<210> 50  
<211> 21  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer  
  
<400> 50  
tggaagtgtg ccctgaagaa g

21

<210> 51  
<211> 23  
<212> DNA  
<213> Homo sapiens  
  
<400> 51  
caaggagctg acttcggAAC taa

23

<210> 52  
<211> 22  
<212> DNA  
<213> Homo sapiens  
  
<400> 52  
agggaagacg atgtggtttt ca

22

<210> 53  
<211> 22  
<212> DNA  
<213> Homo sapiens  
  
<400> 53  
gggacatgtg gagagcctac tc

22

<210> 54  
<211> 21  
<212> DNA  
<213> Homo sapiens  
  
<400> 54  
catcatagtt ccccccagca t

21

<210> 55  
<211> 21  
<212> DNA  
<213> Artificial Sequence

80/88

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 55  
aagcagcacc agcaagtcaa g

21

<210> 56  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 56  
tcatggcctg tgtcagtcaa a

21

<210> 57  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 57  
acatgccagc cactgtgata ga

22

<210> 58  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 58  
ccctgccttc acaatgatct c

21

<210> 59  
<211> 23  
<212> DNA  
<213> Artificial Sequence

81/88

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 59  
ggaattcacc tcaagaacat cca

23

<210> 60  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 60  
agtgtggcta tgacttcgggt ttg

23

<210> 61  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 61  
cagccacaag cagtccagat ta

22

<210> 62  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 62  
cctgactatac aatcacatcg gaat

24

<210> 63  
<211> 21  
<212> DNA  
<213> Artificial Sequence

82/88

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 63  
ccaggtgctc cacatgacag t

21

<210> 64  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 64  
aaacaaccaa caacaaggag aatg

24

<210> 65  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 65  
cgtctccaca catcagcaca a

21

<210> 66  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 66  
tcttggcagc aggatagtcc tt

22

<210> 67  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 67  
gcagaccaggc atgacagatt tc 22

<210> 68  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 68  
gcggatttagg gcttcctctt 20

<210> 69  
<211> 21  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 69  
ggcaccagag gcagtaacca t 21

<210> 70  
<211> 23  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer  
  
<400> 70  
agcctctctg gttctttcaa tcg 23

<210> 71  
<211> 19  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 71  
tggttcacat cccgcggct

19

<210> 72  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 72  
tggctcctca gtagcatcg

20

<210> 73  
<211> 23  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 73  
tgaagttcaa tgcactggaa ctg

23

<210> 74  
<211> 20  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 74  
caggacgatc tccacagcaa

20

<210> 75  
<211> 23  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 75  
tggagtccac gagatcattt aca

23

<210> 76  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 76  
agccttggcc ctcggatat 19

<210> 77  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 77  
cactgagttc gccaaagagca t 21

<210> 78  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 78  
cacgcccatac ttgagaaggg taa 23

<210> 79  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic primer

<400> 79  
gctagtgtatc aacagtggca atg 23

86/88

<210> 80  
<211> 18  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer  
  
<400> 80  
gctggcctct ccgttgag

18

<210> 81  
<211> 22  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer  
  
<400> 81  
tgttcggtgt ccagttccaa ta

22

<210> 82  
<211> 22  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer  
  
<400> 82  
tgccagttgtt agagatggtt ga

22

<210> 83  
<211> 22  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Description of Artificial Sequence: Synthetic primer  
  
<400> 83  
acaactccag gaaggaaacc aa

22

<210> 84  
<211> 19  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 84  
cgaggactcc tgcgagatg

19

<210> 85  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 85  
tgaagaggag tggaggagac ttg

23

<210> 86  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 86  
gaatatgtgg ttctggctca tgaa

24

<210> 87  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 87  
gagaaggagc gatctgctag ct

22

<210> 88  
<211> 23  
<212> DNA  
<213> Artificial Sequence

88/88

<220>  
<223> Description of Artificial Sequence: Synthetic  
primer

<400> 88  
cacgtagaag tgcaggcat cag

23